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THE RECOGNITION OF THORACIC CALCIFICATION*

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WITH the more accurate knowledge of the significance which attaches to primary tuberculous infection, there arises a demand for the satisfactory roentgenographic demonstration of organic evidences of this condition. The ability to recognize calcified nodules and nodes is of importance in such examinations, for by far the greatest number of the demonstrable lesions of primary infection exist in this form.

A comparison of the figures given by several investigators shows a marked difference in the incidence of observed calcification. In this country, Farrell[4] reports the finding of calcified nodules or tracheobronchial nodes in 77.46 per cent of unselected urban patients over fourteen years of age. This figure is based upon the findings in one set of posteroanterior stereoroentgenograms of each patient. Ickert[6], employing roentgenoscopy, found calcified nodules in 58.3 per cent of patients over fourteen years of age in industrial districts in Germany. In school children he reported 20.8 per cent. Stoloff,[17] also by roentgenoscopy, observed evidence of primary infection, either caseous or calcified, in 9.65 per cent of children at the Vienna Kinderklinik. Inasmuch as authentic autopsy records indicate the presence of calcium representing previous first infection in upwards of 90 per cent of adults, it is evident that there exists a weakness in the methods employed to demonstrate the condition roentgenographically, and furthermore, it is evident that the technique and criteria of diagnosis must vary among different observers.

The variations mentioned above suggest a study of the factors involved in the roentgenographic recording and recognition of calcium shadows with a view toward arriving at a standardization of diagnostic criteria and an understanding of the limitations of the examination. The subject presents the following phases.

(1) The topographic anatomy of the lymph nodes and lymphatics draining the lungs and pleura.

(2) The consideration of calcium deposition in the thorax.

(3) The acceptance as a standard of the findings in excised lungs roentgenographed and subsequently examined by sectioning.

(4) The results of the application to a diagnostic series of the criteria for appearance and location as determined above.

(5) A consideration of the causes of the difference between the figures from the two series. (A) Structures simulating calcium. (B) Factors obscuring calcium.

(6) A résumé of factors aiding in diagnosis.

(1) ANATOMY. The topographic anatomy and nomenclature of the groups of lymph nodes of the hila and mediastinum which function as filters for the pulmonary drainage have been the subject of study for numerous observers,[1,3,5,12,15,16,18] and there exist many opinions concerning the exact location and relationship of the various nodes

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as well as a confusing medley of terms for their identification. Fortunately none of the opinions differs sufficiently from the others to result in a serious obstacle to understanding. To Sukiennikow[18] belongs the credit for first attempting to classify and unify the system. Other workers have offered new terminologies and changes in detail. For the present purpose, the topography which is most frequently described and the nomenclature which is briefest will be adopted (Fig. 1). The bronchial lymph nodes are arranged and designated as follows:

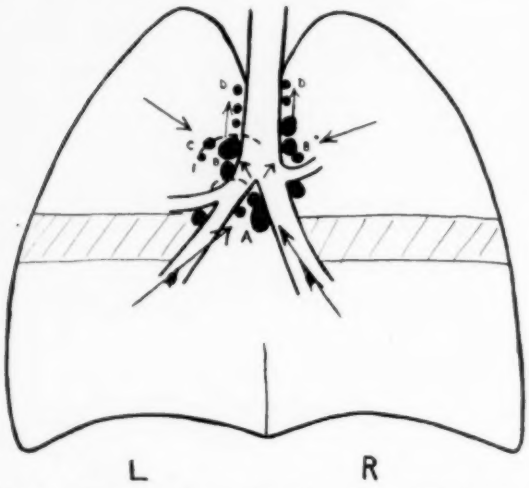

Fig. 1. Topography of lymph nodes draining the lungs and pleura. A. Bifurcation nodes. B. Tracheobronchial nodes. C. Aortic nodes. D. Paravertebral nodes. All others are bronchopulmonary nodes. Arrows indicate direction of lymph flow. Direction from shaded areas doubtful. (See text.)

1. *Paratracheal nodes* (right and left). Small nodes in chain formation, one above the other, on either side of the trachea above the true tracheobronchial nodes.

2. *Tracheobronchial nodes* (right and left). This name is reserved for several large nodes at the right and left of the lower end of the trachea in the angles between it and the right and left bronchi. Those on the left are fewer in number because of the encroachment of the aortic arch on the space occupied by them.

3. *Aortic nodes*. Several medium-sized nodes on the anterolateral surface of the arch of the aorta slightly to the left of the midline.

4. *Bifurcation nodes*. One large and several small nodes beneath the bifurcation of the trachea.

5. *Bronchopulmonary nodes*. All other nodes lying on the bronchial tree. These are always at its bifurcations and lie on the side toward the accompanying artery. True nodes are probably not found beyond the divisions of the larger bronchi[10].

The nodes described above are the filters of the lymph drainage of the lungs.

Knowledge of the intrapulmonary lymphatic system has been established by W. S. Miller and for its details reference should be made to his numerous studies. The system consists of two sets of vessels, the superficial and the deep. The superficial or pleural set communicates with the deep or intrapulmonary set by short connecting vessels equipped with valves which open toward the pleura. Except for the lower surface of the lower lobes, the flow of lymph in the superficial vessels immediately beneath the pleural surface is in the direction of the hilum and eventually into the lymph nodes of the hilum. The flow of lymph in the deep system is through the lymphatics along the pulmonary blood vessels and bronchi toward the hilum and eventually into the lymph nodes of the hilum.[11] The bronchopulmonary nodes are regional for the deep lymphatics. Through them the lymph first passes on its way from the drained lung area to the bifurcation or tracheobronchial nodes. Its further course is described below. It is seen that the flow of both the deep and the superficial lymphatics is toward the hilum. The function of the short communicating branches with the valves pointing toward the pleura is supposedly to care for lymph dammed back by obstruction in the deep system.

The areas of the lungs draining into the various lymph nodes at the hilum and the intercommunication between these lymph nodes are by no means satisfactorily explained. Injection studies by Scott and Beattie[15] suggest that the deep lymphatics

of the upper lobes drain through the regional bronchopulmonary nodes into the tracheobronchial nodes on the right and into either the tracheobronchial or the aortic nodes on the left, while those of the lower and middle lobes drain through the bronchopulmonary nodes in those lobes into the bifurcation nodes. The superficial set follows much the same rule but there is some evidence to indicate anastamosis of vessels of the middle third resulting in an unpredictable direction of flow from this area of the pleura. Ghon[5] agrees with Most[12] in the belief that this rule holds for the deep set as well. Cunningham[2] describes lymphatics from the pleura of the base of the lower lobe passing through the ligamentum pulmonale to the preaortic lymph nodes.

The direction of flow through the mediastinum is probably from the bifurcation nodes upward to the tracheobronchial nodes on either side, but not in the reverse direction, nor is there a well-accepted belief that direct communication exists between the right tracheobronchials and the left tracheobronchials and aortic nodes. Efferent vessels from the right and left tracheobronchial nodes and the aortic nodes pass upward communicating with the paratracheal nodes and eventually end in the thoracic duct or the bronchomediastinal trunk.[1,3,15,16]

Briefly, it has been suggested that drainage from the lower and middle lobes is through the bronchopulmonary nodes to the bifurcation nodes to the tracheobronchial nodes (right or left) to the thoracic duct or the bronchomediastinal trunk either via or avoiding the paratracheal chain. From the upper lobes the flow is through the bronchopulmonary nodes to the adjacent tracheobronchial nodes or the aortic nodes (from the left upper lobe only) and from then on to the thoracic duct or the bronchomediastinal trunk either directly or through the paratracheal nodes. There is probably no crossing from right to left tracheobronchial and aortic nodes or vice versa.

(2) Thoracic Calcium. Calcified costal cartilages are common and are readily recognized by their position. Calcifications in the tracheal and bronchial rings although more infrequent are easily recognized, also because of their characteristic location. Calcified plaques of the aortic arch are similarly identified. Calcifications of old pyogenic empyemata are recognized by their location and the evidences of surrounding pleural involvement, but their differentiation from calcified tuberculous lesions of the pleura is difficult. Broncholiths and phleboliths are uncommon.[13] This is also true of calcium which may lie within neoplastic tissue. The remaining form of calcification in the thorax is the result of healing tuberculous caseation. It is probably the only form of calcification found in a child's chest.

The relationship of calcification to the pulmonary tuberculous process is easily understood if the pathologic sequence of tuberculous infection is followed.

First infection in the lungs is evidenced as a small area of tubercle formation, usually subpleural, which drains into and infects the bronchopulmonary and mediastinal lymph nodes. The lymph node involvement probably corresponds to the direction of pulmonary lymph drainage described above. Commonly the primary focus becomes walled off and assumes a nodular form which is termed the primary nodule. The process in the affected lymph nodes usually becomes circumscribed in a manner similar to the nodule. Caseation is common in either the nodule or the node. It may happen, however, that the primary focus fails to become circumscribed but spreads to larger proportions, even to the extent of lobar involvement. Caseation is then present in varying amounts. In some instances, also, the tuberculous process in the nodes progresses, even in the presence of a healing primary focus. Here caseation is commoner and more extensive than in the healing node. Following the establishment of primary infection any tuberculous process which results from superinfection with tubercle bacilli assumes the characteristics of

secondary infection. One of these characteristics, it is well to bear in mind, is its failure to involve the lymph nodes draining the affected area. This is in direct contradistinction to primary infection. In the lesions of both primary and secondary infection, caseation is found, and it is within healing caseous areas that calcium may be deposited. In both the nodule and node of first infection calcium is deposited in the vast majority of cases. Occasionally calcium is deposited in one and not the other or in neither.

dying of tuberculosis had calcification in 98 per cent of cases, although 25 per cent showed a total area of calcification of 25 sq. mm. or less. In negroes 92 per cent had calcification and 40 per cent showed 25 sq. mm. or less of calcification. These figures were based upon a study of excised lungs and bronchial nodes which had been roentgenographed and subsequently sectioned with extreme care.

The criteria for the recognition of calcification in lesions of first infection were obtained in the present study from the roent-

Table I

	Opie's Figures		Excised Lungs (273 Cases)	Diagnostic Series (1220 Cases)
	White	Negro		
Cases with calcium	98%	92%	69% (188)	24% (288)
Cases with minute calcium deposits only	23%	40%		
Cases with calcified nodules only			16% (43)	8% (96)
Cases with calcified nodes only			18% (50)	11% (131)
Cases with calcified node and nodule			35% (95)	5% (61)
Cases with one calcified nodule			33% (89)	11.5% (139)
Cases with more than one calcified nodule			18% (49)	1.5% (18)
Cases with one calcified node			20% (54)	9% (105)
Cases with more than one calcified node			31% (85)	5% (62)
Total number of calcified nodules			221 (0.8 per case)	182 (0.14 per case)
Total number of calcified nodes			208 (0.7 per case)	193 (0.16 per case)
Total number of calcified nodes and nodules			429 (1.6 per case)	375 (0.3 per case)

Opie's figures represent an accurate standard for the percentage of cases with calcified first infection, regardless of extent and appearance. The Excised Lung figures represent only lesions roentgenographically typical. The Diagnostic Series figures represent such typical appearances demonstrated in living adults (see text).

(3) The Study of Excised Lungs. In order to develop a technique and criteria for the demonstration and recognition of calcified nodes and nodules it was believed advisable to obtain first a theoretically perfect standard for the frequency of calcium and its appearance. For this purpose Opie believes that stereoroentgenograms of excised, exsanguinated, inflated lungs are satisfactory.[13]

The most accurate numerical data on the frequency of calcification in individuals over eighteen years of age are supplied by Opie,[13,14] who states that white adults not

genograms of 400 pairs of excised lungs and the descriptions of these specimens when sectioned. The various appearances on the roentgenogram were identified in this manner.

Following the establishment of criteria for the typical appearance of calcification of first infection the roentgenograms of these 400 pairs of lungs were reviewed. From the total, 273 cases were chosen with no more qualification than that they were of subjects over fourteen years of age and that the lungs had been in sufficiently good condition to give satisfactory roentgeno-

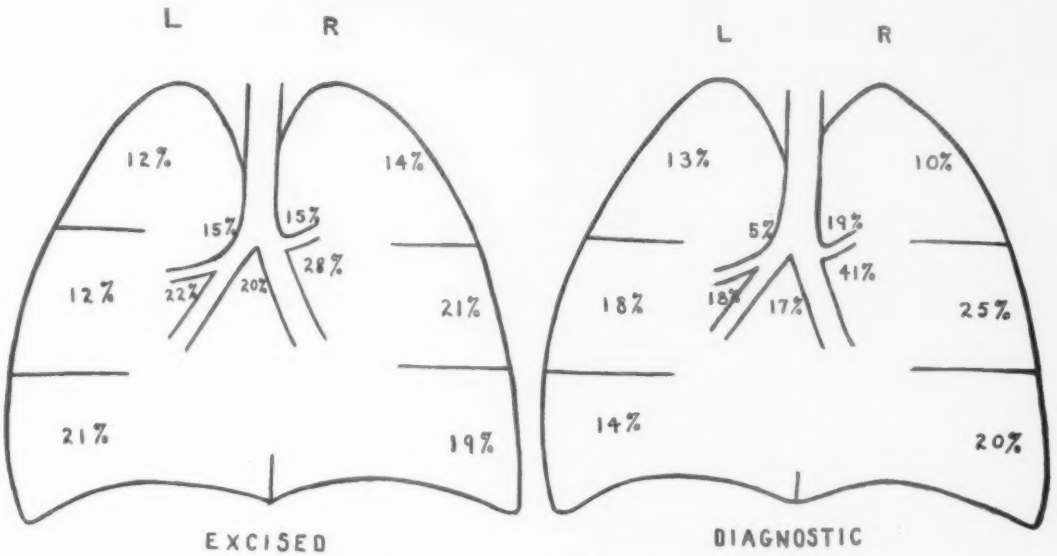

Fig. 2. Comparison of location of typical demonstrable calcifications in the excised lung series and the diagnostic cases. The relative infrequency of nodes at the left hilum region and of nodules at the left base in the diagnostic series is probably explained by the superimposition of the cardiac shadow.

grams. Using the criteria which had been obtained in the manner described above, the shadows which were considered characteristic of calcification of nodule or node were charted. Shadows which were questionable either because of indistinctness or minuteness of size, were not included. The resulting figures (Table 1) (Fig. 2) represent the calcified lesion of first infection roentgenographically typical in the excised lungs of patients over fourteen years of age who had died of all causes and had come to autopsy at five general hospitals in Philadelphia.

As seen in excised lungs the roentgenographic appearance of calcifying caseation is an irregular and mottled shadow. Its earliest appearance is a faint and finely granular density. As the calcium deposit increases the density also increases, usually more markedly in the center, and the granular nature of the shadow becomes a coarse mottling. Complete calcification results in a dense shadow. The periphery is likely to be irregular. The extent of the caseous area largely determines the ease with which calcium deposition in it can be recognized definitely. A large shadow permits the observer to notice easily the characteristic appearance of granulation and irregularity which a minute area will not offer.

Calcification in a healing lesion of second infection is easily recognized. Its situation in the healing lesion identifies its source. The calcium deposits are numerous, vary greatly in size and show marked irregularity in outline.

The calcified primary nodule most frequently is solitary and may exist anywhere in the lung field. When several are present they may be widely separated. There may or may not be accompanying calcification of the hilum nodes, although usually a similar process is observed in both in the excised lungs. On the roentgenogram the calcified nodule shows as an isolated, round, dense shadow, with a slightly irregular margin (Fig. 3). It varies from about 2 mm. to 1 cm. in diameter.

Calcium deposition in bronchial nodes (Fig. 3) is sufficiently extensive in most cases to permit satisfactory observation of its typical appearance described above. On section it is seen that the caseation does not always involve all of the node, nor does calcification always involve all of the caseous area, so that the outline of the calcium shadow need not be that of an entire node.

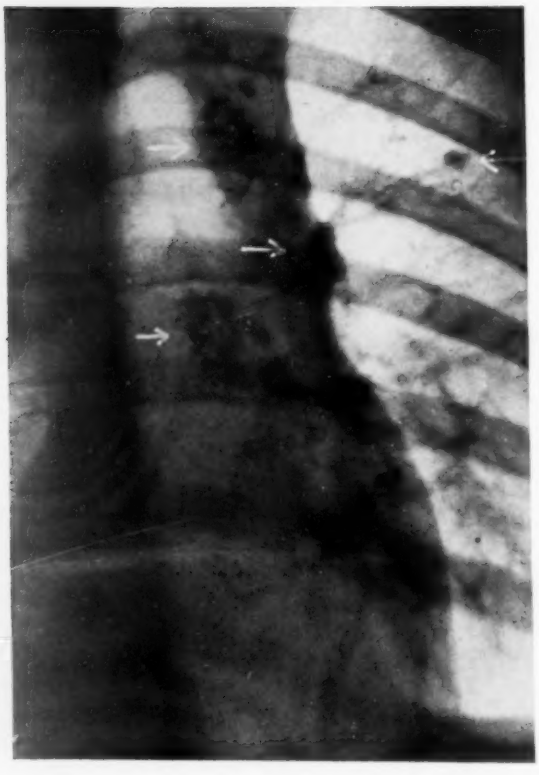

Fig. 3. Typical calcification in three nodes (left) and one nodule (right). Left oblique view. Note the multiplicity, granularity and size of the shadows.

Most frequently, however, more than one node is involved. The shadow of node calcification, therefore, may vary from an irregularly outlined granular density of a few millimeters to a regularly outlined one, node-shaped, of 3 cm. or more. Usually the typical ones measure from 1 to 2 cm. One or several shadows may be seen. The location follows the anatomy.

(4) The Diagnostic Series. In contrast to the excised lung figures are the data obtained from films of living patients over fourteen years of age who have attended the out-patient clinic of the Henry Phipps Institute in Philadelphia. They are members of the group included in the study of tuberculosis in families of the slums. Inasmuch as all members of these families are urged to attend a clinic periodically, it is evident that the major portion of the material consists of cases which otherwise would have had no reason to seek medical attention. Both contact and non-contact families were included in the group studied. On the whole, the group represents a somewhat higher exposure to tuberculosis than does a cross-section of the general population.

Routinely posteroanterior stereoroentgenograms and a left oblique view (right shoulder off at 45°, right arm above the head) were taken. The oblique position shows the region of the tracheal bifurcation and also often establishes the constancy of questionable shadows. All exposures were synchronized with cardiac diastole. The majority of the cases have been examined more than once. The criteria used for the recognition of calcium were those determined from the excised lungs. The diagnoses are based not on one set of films, but on the individual's entire series. It is significant that even with a carefully planned technique, calcium was often definite in only one or two of a number of exposures and rarely except in cases of massive calcification was the shadow typical in all examinations. It was frequently necessary to depend upon the constancy of a shadow in several exposures and positions in order to be sure of its nature. This was usually necessary when distinguishing a nodule from a vessel roentgenographed axially. It was usually necessary to employ the oblique view to demonstrate nodes.

The results of the diagnostic series are shown in Table 1 and Figure 2.

The data from Opie's work, from the excised lung series and from the diagnostic series furnish the following information which may be applied to a general urban population.

1. Over 90 per cent of adults over seventeen years of age have calcified lesions of first infection in the lungs.

2. In at least 23 per cent of adults the total calcification in these lesions is so minute that it only rarely casts a characteristic shadow on the roentgenogram of the excised lungs.

3. In 69 per cent of cases over fourteen years of age there are calcifications of nodules or

nodes or both which cast typical recognizable shadows on the roentgenogram of the excised lung.

4. Most frequently the pathologic process in the nodule and the node is the same, and most frequently one nodule and more than one node are involved but the variations in the pathologic process, extent of calcification and other factors making for demonstrability are so great that any combination of recognizable node and nodule involvement may occur without being cause for comment.

5. With a painstaking technique and accurate diagnostic criteria, calcification of pulmonary first infection in the living individual is recognizable in about one-fourth of all the cases in which it exists, while in individuals with an appreciable extent of calcification it is demonstrated in about one-third of the cases.

6. Less than one-fifth of the total number of calcified lesions of appreciable extent are demonstrated in living subjects. Nodules are less frequently demonstrated than nodes, provided the examination includes a left oblique view.

(5) The Sources of Error. The material in the series of Ickert[6] and Farrell,[4] the excised lung cases reported by Opie, those reported in this study and the diagnostic series of the Phipps Institute are of sufficient similarity to confirm the previously stated belief that the marked differences in the reported figures of roentgenographically observed calcification are due to technical factors and the failure to use proper diagnostic criteria.

Granted that the studies of excised lungs in this laboratory have established accurate diagnostic criteria, there exist two sources of error. These are (*a*) structures simulating calcium and (*b*) structures obscuring calcium. Both militate more strongly against the recognition of small calcifications than against that of larger ones.

(*a*) *Structures Simulating Calcium.* The forms of thoracic calcium other than that of nodule and node origin have already been discussed. Solitary fibrous or fibrocaseous nodules in the lung parenchyma may cast a shadow simulating a partially calcified focus. Usually the differentiation is of so little practical value that it need cause no worry.

Most common of all factors simulating calcium in the chest is the shadow of a blood vessel roentgenographed axially. An understanding of the frequency of this phenomenon and its appearance is a requirement for the diagnosis of node and nodule calcium. Absorption of roentgen rays varies directly with the total density of the exposed substance. It is theoretically possible that the same amount of roentgen rays can be absorbed by a centimeter or two of a filled blood vessel roentgenographed axially and by a calcified nodule a few millimeters thick, and shadows resulting upon the film will be of equal density. Furthermore, the contrast on the film of the shadow of a structure with the shadows of surrounding structures varies directly with the difference in total density of that structure from the total densities of the surrounding structures. Therefore a calcification will cast a shadow of sharp contrast against that of air-bearing lung tissue but it will cast a less noticeable shadow in those areas of the pulmonary fields where greater density of surrounding tissue occurs. Within the hilum or the region of the basal trunks the contrast of the shadow cast by calcium is likely to be less sharp. The same conditions hold good for the shadows of axially roentgenographed vessels. As for structures whose elements present no relative increase in atomic number and whose form presents no relative increase in dimension to the penetrating ray, their inability to cast a distinguishable shadow in the hilum is obvious. McPhedran and Weyl[9] have shown that into this group fall uncalcified lymph nodes, normal or caseous. Their only chance for recognition lies in the chance of their encroaching upon air-bearing lung tissue, and this presupposes enormous enlargement.

Practical proof that axially radiated vessels are responsible for an appearance which simulates calcium in the roentgenogram was found in the study of a number

of excised lungs.* Before removal, the pulmonary vessels on one side were tied off. After removal, the unligated lobes were drained. The lungs were then inflated with

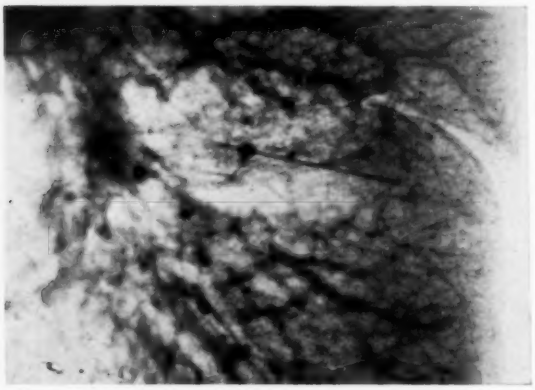

Fig. 4. Vessel shadows in a roentgenogram of an inflated normal lung. Pulmonary artery ligated before excision.

the ligatures still in place and stereoroentgenograms were taken of them.

Invariably the appearances of the two sides differed. The ligated side showed a dense hilum shadow. Radiating from it were heavy basal, paravertebral and first interspace trunks plus the typical vascular shadows. The lung markings were definite. In decreasing frequency and size from the hilum outward there were always numerous shadows of varying but individually homogeneous density, many rounded and many slightly irregular (Fig. 4). The rounded ones possessed a clear-cut regular margin. Almost always the shadows were in both films of the stereoscopic pair. They occurred upon a trunk, vessel or lung marking, and they were of the same width as these markings. They were rare in the outer third of the lung field except when heavy lung markings or trunks were present in this region. These shadows were the same as those observed in the living lung. In contrast, the unligated side showed a hilum shadow of very little density. The lung field was clear, the trunk and vessel shadows were absent except for a suggestion of the basal trunk markings and the lung markings were extremely faint. No nodular shadows were seen except in the region where basal trunks sometimes persisted, and here they were only suggestions of increased density. Careful sectioning of the lungs revealed no difference in the structures on the two sides producing the appearances described above, other than the presence or absence of blood in the pulmonary vessels.

The above findings corroborate those of McPhedran and Weyl.[8]

A frequently mentioned point of differ-

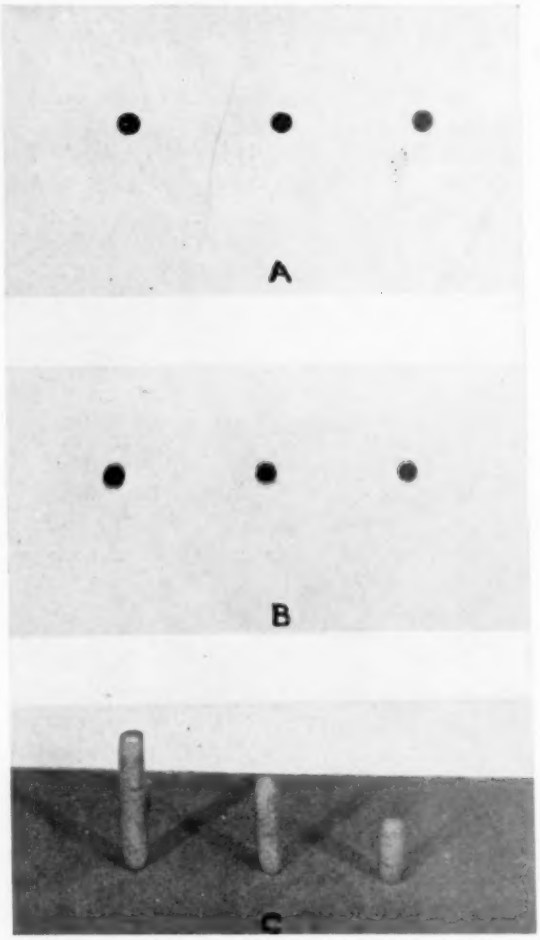

Fig. 5. C. Straight paraffin cylinders 4 mm. in diameter. A. Roentgenogram made with central ray axial to cylinders. B. Roentgenogram made with tube shifted 12 inches. Film-target distance 50 inches.

* The specimens were obtained from the Laboratory of Pathology of the Pennsylvania Hospital through the courtesy of Dr. John Bower.

entiation between the calcium shadow and that of the end-on vessel is the failure of the latter to appear in both films of a stereoscopic pair. The shift is supposed to alter

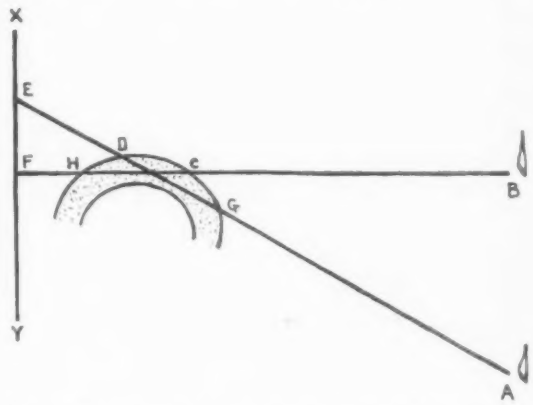

Fig. 6. Exaggerated diagrammatic proof that curved vessels may present the same length ($HC = DG$) to the rays in both exposures of a stereoscopic pair. (Modified from McPhedran.)

the direction of the rays sufficiently to eliminate the end-on effect. This is not the case. Stereoroentgenograms of the excised lungs with ligated vessels showed the shadows to be present almost always in both films. Occasionally one was more irregular than the other, but quite frequently no difference in outline was noted. To demonstrate that the usual tube shift of 5 inches at a 50-inch distance is insufficient to destroy the end-on phenomenon in one film when the shadow shows clearly in the other, it was decided to make stereoscopic films of several straight paraffin cylinders with a diameter approximating that of a medium-sized pulmonary blood vessel (Fig. 5, c). The first exposure (Fig. 5, A) was made at 50 inches with the tube directly in line with the axis of the cylinders. All three cylinders show as perfectly circular shadows varying only in density proportional to their length. The second exposure (Fig. 5, B) was made at 50 inches with a 12-inch shift. The resulting shadows of the cylinders are very slightly irregular. It is evident that the shadow of a straight vessel of medium diameter is very little distorted by a 5-inch shift.

The blood vessels of the human lung, however, are characteristically slightly curved. That the shadow obtained from roentgenographing a curved vessel axially may not be altered at all by a stereoscopic shift has been suggested by McPhedran[7] (Fig. 6). One can appreciate from the diagram that the length of vessel presenting axially to the ray can be exactly the same regardless of the magnitude of the shift, provided the direction of the shift is at

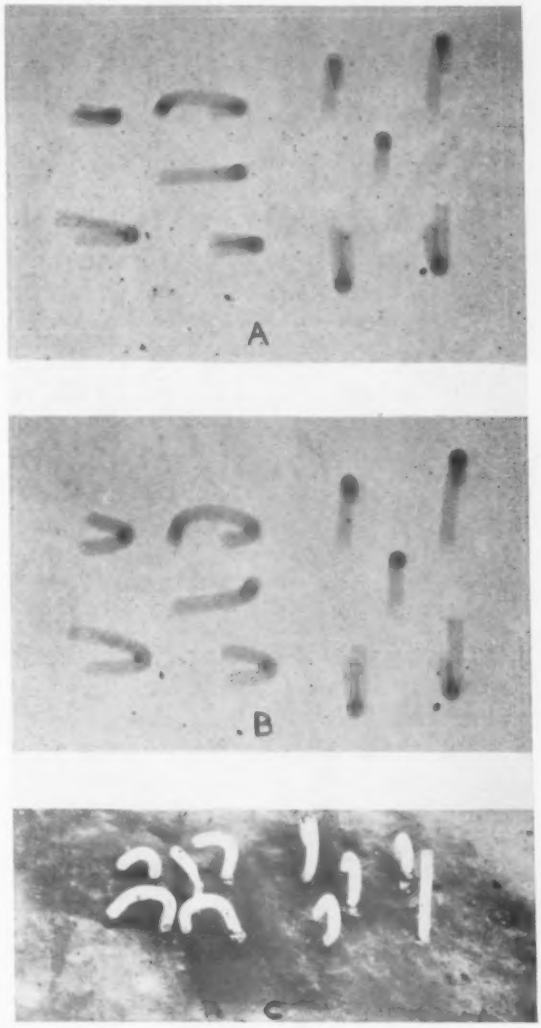

Fig. 7. C. Curved paraffin cylinders 4 mm. in diameter. A. Roentgenogram made with central ray axial to all cylinders. B. Roentgenogram made with tube shifted 12 inches at 90° to curve of cylinders on left. Film-target distance 50 inches. (See text.)

180° to the curve of the vessel. Two sets of curved paraffin cylinders were arranged with their curves at 90° to one another (Fig. 7, C) and stereoscopic exposures made (Figs. 7, A and B), again with a 12-inch shift. The end-on shadows of the curved cylinders on the left lying at 90° to the direction of the shift are slightly distorted in the second picture (Fig. 7, B). Those of the cylinders on the right parallel to the direction of the shift are not affected at all.

It is evident that pulmonary blood vessels roentgenographed axially cast shadows which may simulate those of calcium. These shadows have the following characteristics.

1. Typically a clearly defined, circular outline. Surrounding structures or tangential radiation may destroy this, however.

2. A smooth, homogeneous density which varies in intensity in different shadows.

3. A correspondence in number and size to the vascular distribution in the lung.

4. Situation along a faintly visible vascular shadow.

5. A tendency to be reproduced in both films of a stereoscopic pair, but a failure of the same vessel shadows to be reproduced in films taken in different positions of the patient.

(*b*) *Factors Obscuring Calcium.* The superimposition of the thoracic cage, the diaphragm and the intrathoracic organs of a greater density than the lung upon the lung fields and the hilum regions is the factor chiefly responsible for the inability to demonstrate calcification in more than a fourth of the existing cases. Because of the heart, the left hilum region is seen with difficulty even in oblique views. It should be mentioned here that the tissues of children offer less resistance to the roentgen ray than do those of adults, and in consequence one is frequently able to observe clearly the characteristic shadow of calcification showing through the shadow of the heart or mediastinum in a roentgenogram of a child's chest. In the case of adults, because of the denser tissue, this is rarely seen.

The dense shadow of the hilum, mostly due to blood vessels, is so irregular and so confused by the shadows of vessels roentgenographed axially that the diagnosis of calcification in this region is almost impossible except in an occasional case.

Blurring by movement, mostly of heart and vessels, results in a loss of detail which can best be overcome by speed of exposure and synchronization during cardiac diastole.[8,9]

Smallness of a calcium deposit frequently accounts for its being masked by surrounding tissue. For this reason more nodules than nodes escape recognition. The frequency of minute calcifications is well demonstrated by Opie's figures.

(6) A Résumé of Factors Aiding in Diagnosis. A fundamental knowledge of the anatomy of the chest, of the pathogenesis of node and nodule calcification, and of the other sources of thoracic calcium is desirable. With this foundation plus an understanding of the appearance of the shadows cast by calcium and by blood vessels the following points in technique will prove helpful.

(*a*) Speed in exposure.

(*b*) Synchronization of exposure with diastole.

(*c*) Stereoscopic examination.

(*d*) The left oblique view. This view is of assistance in examining the mediastinal area. For example, only 14 per cent of the cases showing calcification of the bifurcation nodes were diagnosed from the postero-anterior view alone.

(*e*) Possibly the employment of the roentgenoscope. Here only calcifications of appreciable size can be seen and in the hila the phenomenon of curved, axially roentgenographed vessels often makes establishment of a shadow's identity difficult even with much rotation. The chief value of the roentgenoscope lies in discovering calcifications in regions not well demonstrated on the films of routine positions.

CONCLUSIONS

With a technique of examination based upon careful study, calcification of tuberculous first infection in the thorax is demonstrable roentgenographically in only about one-fourth of the existing cases.

The superimposition of structures of varying density, the factor of cardiac and intrapulmonary vascular movement and the minute size of many of the calcium deposits are responsible for this.

Blood vessels roentgenographed axially produce shadows which may be confused with those of calcium.

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THE USE OF OPAQUE OILS IN THE DIAGNOSIS OF MAXILLARY SINUS DISEASE*

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IT IS only within the past five years that opaque materials in sinus visualization have come into common use. A few earlier references to it are found in the literature. A contrast medium of an aqueous mixture of lead sulphate was used by Weil[17] in 1902–1903; in 1919 Beck and Ramdohr[2] made injections with bismuth; a 15 per cent solution of potassium iodide and a 20 per cent aqueous solution of barium sulphate was used by Brunetti and Filippini[3] and reported in 1924.

Our interest in the use of opaque media for diagnosis in maxillary sinus disease dates back to April, 1925, when we were called upon to make roentgenograms of a case suspected of having polypi. The primary film showed suspicious shadows in the base of the right antrum (Fig. 1). An injection of 4 c.c. of 20 per cent aqueous solution of neosilvol was made through the normal opening into this antrum (Fig. 1*a*). Van Osdol[15] has reported the result of this and several other cases upon which the same investigations were made. He found the method particularly helpful in antral cases where the findings were not definite.

In 1921 Sicard and Forestier[13] used iodized oil in injecting body cavities. Since there is no free iodine it is well tolerated in the cavities of the body, at the same time offering an excellent contrast medium.

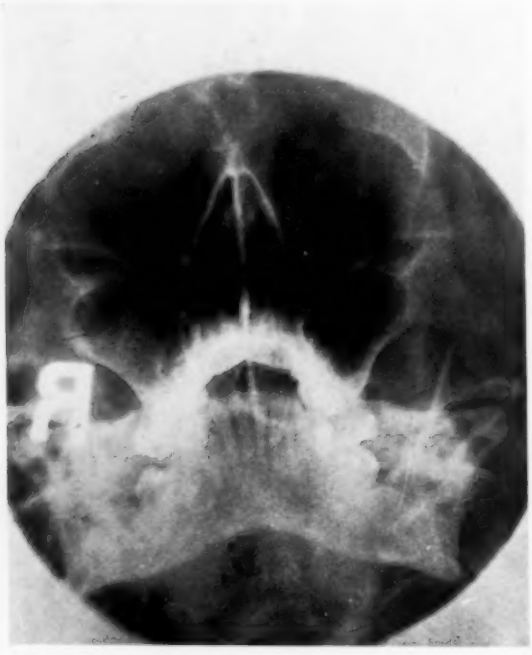

FIG. 1. Probable polyp or cyst in right antrum.

FIG. 1*a*. Neosilvol injection outlines polyp.

During the time of our investigations with neosilvol, two otolaryngologists, Reverchon and Worms,[12] reported in March, 1925, a number of cases wherein the diagnosis had been aided by the injection of iodized oil into the eustachian tube, esopha-

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gus and paranasal sinuses. The medium used was lipiodol, an extract of poppy seed having an iodine content of 40 per cent. Since 1925 a number of authors have written favorably of its use. For the past four years we have used some form of halogenated oil exclusively in our sinus contrast work, and during this time have had the opportunity of studying more than 300 cases. The halogenated oils have sufficient viscosity to remain in the sinus long enough to insure study and remove themselves automatically.

The injections in the cases seen by us have been done in the offices of otolaryngologists, many of whom are a considerable

Fig. 2. Normal left antral injection, posteroanterior view.

distance away. Once the antrum is well filled, there has been no trouble in its retaining the injection, with the exception of a few cases where window operations had been done. In these it has been found advisable to plug the windows with a small piece of cotton.

After following a number of cases for several days we concluded that no valuable

Fig. 3. Normal left antral injection, lateral view.

information was to be obtained from visualizing the sinus drainge. E. Lloyd Jones[8] says that an emptying time of more than forty-eight hours means a pathological interference with the drainage mechanism. Many of our follow-up films show a retention of a large part of the medium for four or five days (Figs. 4 and 9). Proetz[10] states that the maxillary sinus drainage is somewhat slower than the other sinuses, while Weil's[16] cases emptied within one or two days. This difference is probably explained by the difference in technique or materials used.

There has been some controversy as to whether or not the antrum should be washed out before the oil is injected. Goodyear[6] thinks that it should not be recom-

Fig. 4. Same case as Figures 2 and 3, six days later, showing oil retention with typical mucous membrane reaction. Patient without symptoms during this time.

mended because of a possible edema, while MacCready[9] washes the antrum with saline then carefully dries it before the oil is injected. Since the oil is insoluble in water it is obvious that the antrum should be dry if we are to obtain a true outline. Our best results have been obtained when the injection was done before or several days after washing.

MacCready says that there may be a feeling of fullness in the cervical glands for a short time after the oil injection, due to absorption by the lymphatics, and Anderson[1] mentions the possibility of a fatty embolism if oil is introduced between the mucous membrane and the bone. There is undoubtedly a change in the mucous membrane after the oil has remained a few days, but this does not cause any alarm (Figs. 4 and 9). A few cases have had symptoms similar to those in acute coryza. We have not seen, nor have we found in the literature, any complications of importance after the oil injection. In fact, many of our patients report considerable relief for several days afterward.

It has long been known that the maxillary sinus can change its appearance, as seen on the roentgenograms, within a few hours. This may be due to an allergic reaction or to an infection. We have seen one case where only a small amount of oil could be injected into the sinus, followed by a later injection which completely filled a normal antrum (Figs. 11, 12, 13 and 14). Jones[8] and Proetz[11] refer to this and warn against radical measures before conservative treatment followed by check injections. We have been unable to find other mention or this in the literature. Proetz[11] has recently described 3 cases in which the injected antra were normal but in which the films four or five days afterward showed a definite thickening in the mucosa, which extruded most of the oil. Since these reactions occurred in known allergic individuals

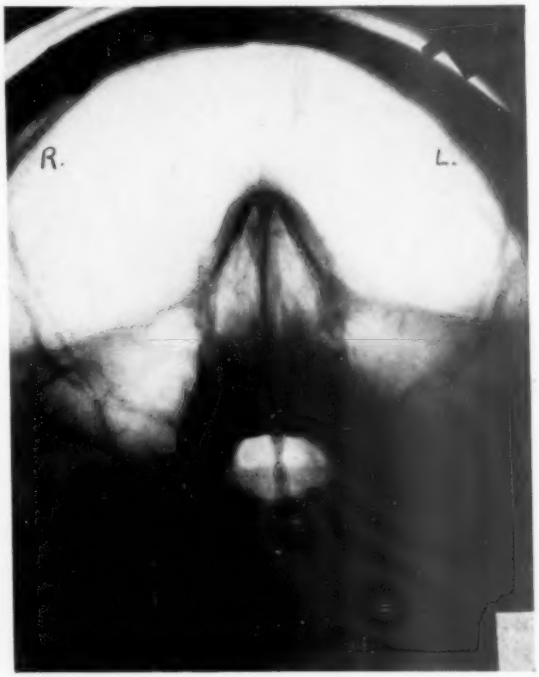

Fig. 5. Left maxillary shows partial opacity.

Fig. 6. Same case as Figure 5 injected. Note that pathology is less than suggested on Figure 5.

Fig. 7. Lateral view of Figure 5, practically normal.

Fig. 8. Injection of right maxillary. Regarded as normal.

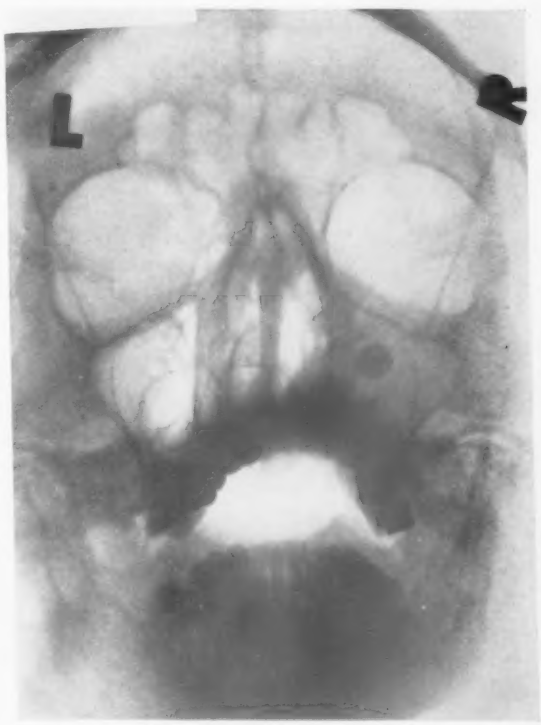

Fig. 9. Same case as Figure 8 four days after injection showing small globule of oil at ostium and mucous membrane thickening.

FIG. 10. Lateral view of Figure 9.

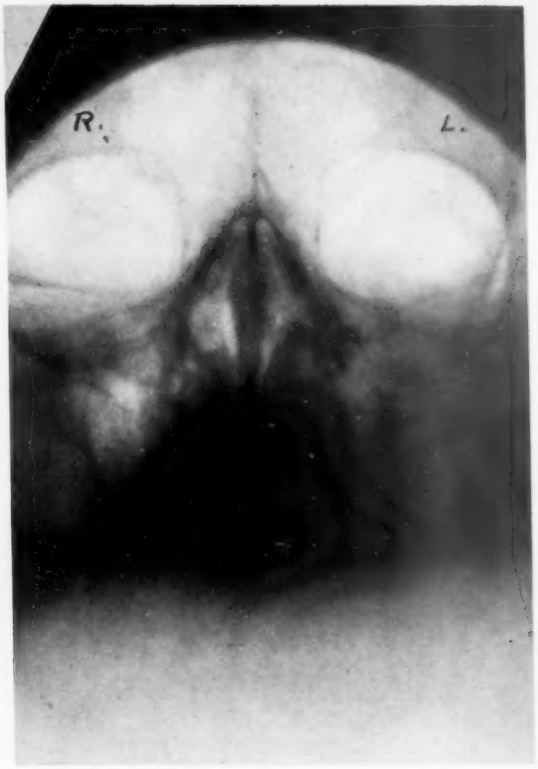

FIG. 11. Symptoms of acute left maxillary sinusitis. Oil shows decided thickening, very little air space.

FIG. 12. Lateral same case as Figure 11.

FIG. 13. Normal. Same case as Figure 11 six weeks later. Had had three irrigations. Symptoms disappeared. Case shows value of close cooperation between rhinologist and roentgenologist.

he believed them to be the result of an allergy. This reaction has been present in about 20 per cent of his cases. We have taken films on many of our cases four or five days after injection and in almost every case this reaction has been present (Figs. 4 and 9). It does not seem likely that an allergy would explain the reaction when present so often. It may be that the oil is extruded from the antrum by this means.

Fig. 14. Lateral view. Same as Figure 12.

In order to obtain the greatest amount of information from the examination, the antrum should be well filled. We have not attempted to have the injected oil measured as the size of the sinus can be judged from the films. The amount of the oil retained by the normal sinus varies from 6 to 12 c.c.

We have not found that making a number of films in different positions is necessary. In the well-filled antrum an erect posteroanterior and lateral film, taken in

Fig. 15. Small right antrum with marked thickening. Partial loss of eyesight.

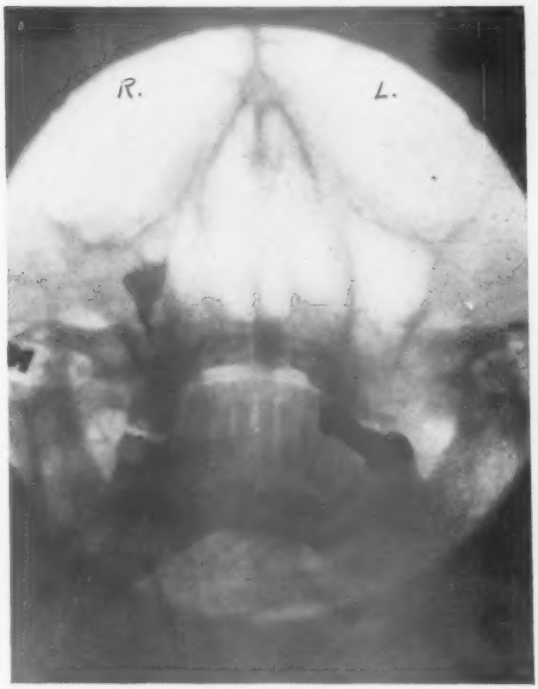

Fig. 16. Injection same case as Figure 15 showing thickened mucous membrane.

Fig. 17. Lateral view showing same as Figure 15. Operative findings suppurative sinusitis.

the regular antral position, as given by Israel,[7] is usually all that is necessary. Lately, we have been using an erect posteroanterior position in which the horizontal central ray passes along the floor of the antrum (Fig. 21). We have found this to be the most helpful of all posteroanterior exposures. In the partially filled antrum it is often necessary to use several positions in order to visualize all the pathology. We insist on primary films and also insist that only one antrum be injected at a time. With both injected the value of the lateral view is, for the most part, lost.

There are, at the present time, a number of satisfactory preparations on the market. The greater part of our experience has been with lipiodol, diluted 33 1/3 per cent in olive oil. The results with brominol and campiodol have also been good. Glaser, Futch and Snure[5] have used the latter altogether, with excellent results. Those interested in the chemical and pharmacologic tests of halogenated oils are referred to the work of Tabern, Hansen, Volwiler and Crandall.[14]

Fraser,[4] after a study of 35 injected antra, concluded that: (1) one may demonstrate that an antrum is without abnormality; (2) in acute inflammation, one may throw light on the pathological process; (3) in more advanced cases, one may obtain indications for surgical treatment, i.e., continuation of irrigation; (4) in chronic hyperplastic cases, one may show what must be accomplished at operation, and (5) invasion of the sinus by dental cysts and other pathological processes may be diagnosed. Fraser's forecast has been amply verified.

The normal antrum, when injected, will show a thin line of separation, not more than 1 mm. between the oil and the sinus wall (Fig. 2). At the base one may find variation in the oil outline, due to projection of the tooth roots, but the curves will be smooth and correspond to their outline,

Fig. 18. Right antrum shows large filling defect with an irregular marginal outline. Continuous nasal discharge, general malaise with nasal obstruction.

Fig. 19. Lateral view, same case as Figure 18. Operation showed cystic abscess in mucosa, polypoid degeneration.

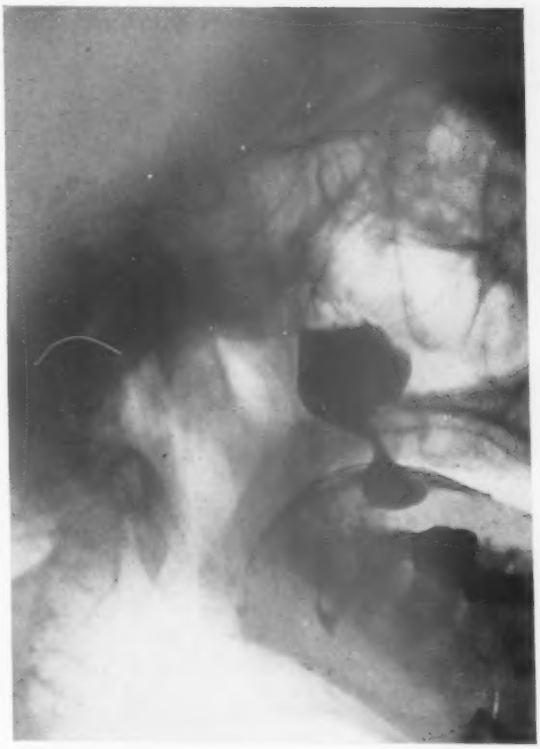

Fig. 20. Injected dental cyst. No oil in antrum. Continuous discharge after tooth extraction. At operation cyst found separated from antrum.

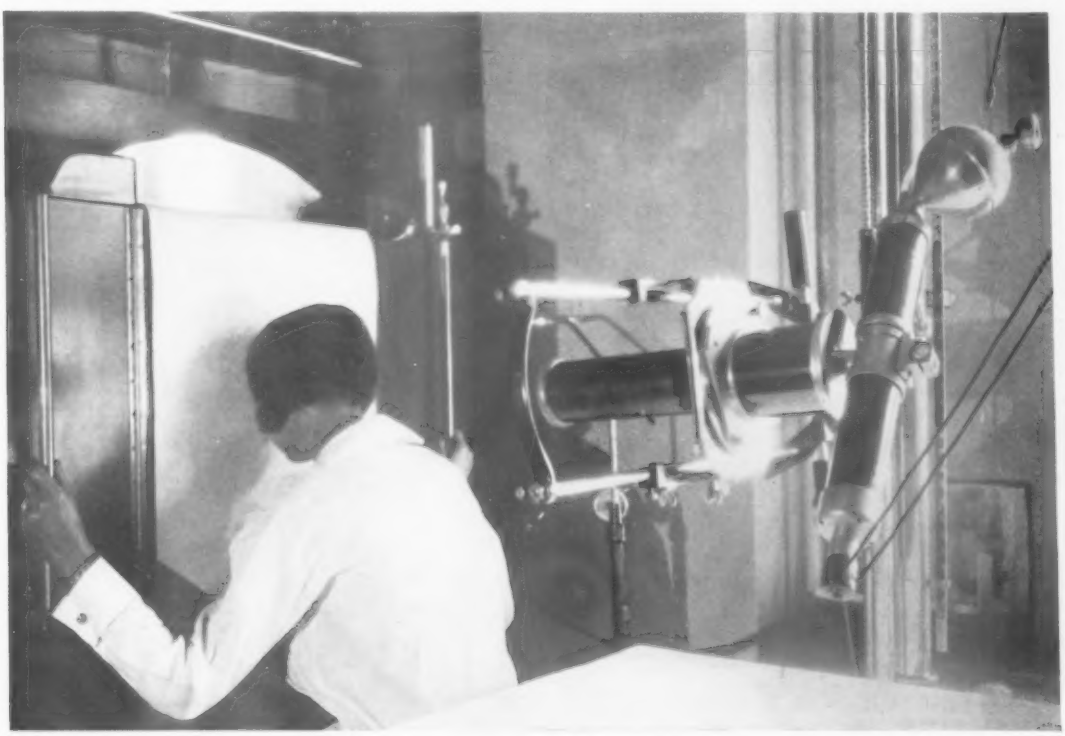

Fig. 21. Usual position used in posteroanterior projections to show the floor of the antrum.

unless there is disease (Fig. 14). Polypi will produce a smooth localized defect in the filled antrum and their exact size and location can be determined by proper projections (Figs. 18 and 19). Cysts and mucoceles give somewhat the same defect, are usually larger and more circumscribed. Hyperplastic changes produce an irregular outline, varying from slight changes to those where only a few drops of oil are retained near the central portion of the antrum (Figs. 16 and 17). Despite these pathological changes a great many of these cases return clear washings.

CONCLUSIONS

1. The use of opaque oil enables the visualization of the actual pathology present in the maxillary antrum.

2. It determines better than any other means, the type of treatment to be instituted.

3. The oil can be injected without harmful effects.

4. Injection is indicated in those cases where the primary plate is inconclusive.

5. There is usually a reaction of the mucous membrane, lasting until the oil has been extruded.

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DISCUSSION

Dr. F. V. Overman, Indianapolis, Ind. This is rather unexpected. We as otolaryngologists came to West Baden today because we knew we would learn something. This paper we have not heard by Drs. Beeler, Smith and Collins. We have a very extensive experience in Indianapolis in this work. I know of nothing that has been developed by roentgenologists in recent years that has been of more value to otolaryngologists than the oil injection. Before we began using this injection, we were in a quandary in many cases as to a diagnosis and as to treatment. I think often we failed to do surgery when we should have done it and many times we did surgery when it was not indicated.

One case that Dr. Collins showed on the

screen was the left antrum, which happened to be a case of mine that had had some very serious trouble. We injected her antrum, and I was able to get a very small quantity of oil into the left maxillary sinus. Naturally, I supposed that that antrum was filled with thickened mucous membrane or some other pathology.

Within the next two weeks, I irrigated that antrum twice, or three times I believe. We then had a film made again and found practically a normal maxillary sinus. I can't explain that to you. You know about that better than I. This was a case where before oil injection surgery would have been suggested immediately. That has been about two years ago. That patient is well now and has had no trouble since. Whether the oil is curative, I don't know. Some of our men think that it is.

The greatest difficulty I have had has been the injection of oil in antra that have windows. However, we have devised some methods by which we can keep the oil in the antrum while the picture is being taken Just what is to be developed here, I don't know. It is for your roentgenologists to help us. I think that the mistake is often made in irrigating an antrum before it is injected. I have never done this. I have seen some films where this was done, and I thought the picture was not so helpful as it could have been if the oil had been injected without irrigation. Not all of our men agree on this point, however. But it is going to be with the help of roentgenologists, I think, that we are going to gain some real information and some real help.

Dr. D. O. Kearby, Indianapolis, Ind. The views that I shall express will be very short and must naturally and essentially be those of a practical rhinologist. In thinking about sinusitis, I have worked out, satisfactorily to myself, a classification in which I think of them as acute, subacute or chronic.

In an acute suppurative sinusitis, I rarely ever, I should say never, use the roentgen ray. It isn't necessary. Any individual who catches a cold and has it two weeks, can scarcely get his breath, has some headache, and a lot of discharge, does not need a roentgen examination to know that he has suppuration in his accessory sinuses.

The subacute I think of as that type of sinusitis in which there has been an element of more time elapsed. For instance, the patient comes in two months, three months after the onset of his influenza. Rarely do I use the x-ray in making a diagnosis of this type, because I can satisfy myself by the history, the clinical findings and what I can get from the sinuses by irrigations. However, sometimes we do use the x-ray in this type and the point that I would make about this particular type of sinusitis to roentgenologists, would be how essential it is that they know the history of this case before they read chronic pathology in the sinus, because in this subacute case you will have a lot of apparent damage done to the lining membrane, that is, it will be thickened. If you report a lot of damage, someone will do a radical operation when it is not indicated. This thickened membrane will return to normal under appropriate treatment other than surgery.

Now we come to the chronic case, one that has been going on for a long time, a year, five years or ten years, in which there has been a tremendous amount of infiltration of connective tissue into the lining membrane of the sinus, permanent damage done in which you have polyps or permanent thickened membrane, etc. I don't think that any roentgenologist could satisfy me from a reading of the primary film, of the pathology present in such a case. I will always want some of the opaque mixtures used in these chronic type cases. I used to think that putting lipiodol into this type case told me two things, first, the essential thing, the amount of damage that had occurred to the lining membrane of the sinus. Second, I was led to believe that I would know something about the drainage from the sinus, measured by the time that it took the lipiodol to disappear. Our experience, in going over these lipiodol injected cases, as Dr. Collins brought out in his paper, is that in practically every one of them, where we did not have a thickened membrane, we had a swelling or reaction. If the lipiodol is going to set up a reaction in the antrum itself, it is fair to presume that it sets up the same reaction in the normal ostium of the sinus, and as a consequence, it would not empty very freely. In fact, in chronic sinusitis, there are only about two things that are being discussed now by the otolaryngologists and one of them is whether you shall use these opaque mixtures for diagnosis and the other one is whether you shall curette out all the membrane or not. The latter you are not interested in, but I do feel if you are not using or suggesting or offering to help your otolaryngologists at home by the use of opaque

mixtures, you will do them a great favor by convincing them of their value.

Dr. J. W. Carmack, Indianapolis, Ind. The subject of visualization of the sinuses with opaque solutions has been one of the refinements, to me, of x-ray in sinus work that has added more assurance than probably any other one thing. You all know, as well as we do, that the treatment of sinusitis is not an unqualified success. It seems that there is now the tendency among otolaryngologists to do either a very palliative treatment or to do a thorough radical treatment. It seems that if we do not get results with a palliative sort of treatment, then our best results are had by thorough cleaning out of infected tissue. Our poor results, we feel, are largely due to infected or diseased tissue remaining in the sinus. I say this in spite of the sporadic or endemic views that we have toward partial operations.

This visualization of the pathology in the sinuses has done more for me in going to an individual and telling him that he has a certain definite thing and that I can promise him certain things, than any other refinement that we have had in the study of the chronic sinus diseases. So if we are to get the most from such a thing as you have given us, we must have a standardization not only of your technique, but we must have a standardization of the preparation of the patient so you will know what has been done. You must give us a standardized technique as nearly as possible so we will know what you have done, because it is only by the transmission of what you can tell us through us to the patient that any of these things are going to be valuable.

It is obvious that not all cases need injection with lipiodol. The acute inflammations, of course, are eliminated. There are many of the chronic types which do not mean lipiodol injection, but it seems to me those of us who have used it are beginning to depend more and more upon it and use it in a greater number of cases, so we select the chronic cases without exacerbations as the ones per se in which we will get some knowledge with injection of this fluid.

In many cases the primary film is sufficient and some roentgenologists, I understand, claim that they can tell anything about a primary film which can be told about one taken after injection of lipiodol. That may be very true for you, but that is not sufficient to transmit that knowledge to me. It is the borderline cases, particularly, without massive pathology in which we probably get the most value, because the large infected cyst or large polyp will show. In those cases fall the cardiac, the renal, and many of the other low-grade chronic conditions such as neurasthenia, so-called, or the neurasthenic cases, I recently ran across some literature in which in 1600 A.D. some man wrote a wonderful description of the man who forgets, the man who is lethargic, who cannot concentrate, the man whom we have classed as a neurasthenic, as being due to too much mucus coming from the upper respiratory tract. It is in those so-called neurasthenics that we are going to get great value from this particular type of work.

In selecting these cases, one must be on guard at all times for the allergic type. I have not seen the conditions described by Proetz of St. Louis, but I can understand how it could be very possible to have in the true allergic case a swelling of a mucosa of considerable amount, hardly to the extent of filling the entire sinus, but a considerable amount of swelling from the injection of this irritating iodine preparation. To that case it is extremely irritating where it may not be at all irritating to the normal individual. But that is our job. We have no business sending an allergic case to you injected with lipiodol and expect you to give us any sort of an intelligent reading. That case should be culled out or should be classed as an allergic when he is injected and sent to you, and we should expect any sort of bizarre result.

The next thing in my mind is the preparation for the roentgenogram. It has been said that there is a question or a discussion as to whether or not these cases should be irrigated. It is my plan to irrigate in all cases before injecting the lipiodol and sending them to the roentgen laboratory. I have not seen bad results. It is possible if that case had fluid put in there and left for an hour or so, you may get a reaction, but you always have the possibility of thick, viscid pus being in the sinus. I can easily understand how this case shown by Dr. Collins, in which there is only a small amount of the lipiodol showing and later another taken where the cavity shows normal size, there might be (I don't say it is true in this case) thick, viscid pus, which I have seen and have had to wash out several times in order to clean the mass out. I wash the sinus and dry it thoroughly. This must be done by the postural method, the head to one side and air blown through the sinus. They

can be dried out very thoroughly. It has been very satisfactory, at least to me. I think most of these sinuses should be injected through a needle under the inferior turbinate, through the lateral wall of the nose. I don't think we should be satisfied with attempting to fill many of them through the normal ostium, because we are not always sure when we use that method and repetition may be necessary.

Also, we know that if there is a small amount of pus, if we have a subacute chronic condition, the pus tends to form in globules or rounded masses in the floor of the sinus. It is perfectly possible for those rounded masses to remain in that floor and visualize as a mucocele or a polyp. Those can be washed out and, in my opinion, should be.

Another thing we should fill these sinuses as full as possible and keep the oil in. It is always possible where windows are present to use wool packing and prevent loss of a great deal of the fluid, but the better we have them filled, the fewer number of positions we will have to take and the better the result.

I like a heavy oil which has to be used through a fairly large needle. The thinner the oil, the more oil will be lost between the time of injection and the time of taking the roentgenogram. The light oil is most satisfactory in the visualization of the other sinuses, such as the sphenoid or ethmoid, which, of course, do not come in this paper, but which are filled by the displacement method as described so well by Proetz.

I think the only other thing I shall say is that I am very pleased indeed to see the methods being used by roentgenologists to improve the pictures that we are asking for in children because certainly your troubles are ahead of you. It is my opinion there will be many more requests for x-ray of sinuses and mastoids in children in the future than there have been in the past.*

* For further discussion, see page 220.

THE NASAL SINUSES: ROENTGENOGRAPHIC AND CLINICAL OBSERVATIONS*

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THE *Quarterly Cumulative Index Medicus* list of approximately one hundred and fifty articles for the past year is ample proof of the general interest and value of the study of sinus pathology.

Sinusitis has been recognized as a clinical entity for many years. In recent years the roentgenographic examinations have made definite advancement in the refinements of the diagnosis of this clinical entity. The marked advancement of this specialty has been accomplished by the cooperation of the rhinologists and the roentgenologists.

Sinusitis may, for all practical purposes, be classed as acute and chronic. The acute type is manifested by empyema, allergy and as the result of trauma. The chronic type includes the sinusitis with polypi, cysts or mucocele, hyperplastic membrane, the sclerotic bone changes, and the chronic empyemas. The benign bone tumors and malignant new growths need not be included as a type or group of sinusitis. However, a differentiation of these growths is of importance to the surgeon.

The benign bone tumor is not frequently encountered, is easily recognized and is of little significance.

The malignant growths in and about the sinuses are, of course, vitally important and must be accurately differentiated if possible. The bone changes in malignant neoplasms are fairly typical in the majority of cases. Their incidence is not frequent but the gravity is of such importance that in each and every instance a biopsy should be taken.

Another very important involvement of the sinus is syphilis. Congenital luetic manifestations in sinuses of children are frequently encountered in some clinics. These sinuses so involved are very characteristic and may often be diagnosed even without a Wassermann test.

The luetic involvement of the sinuses is

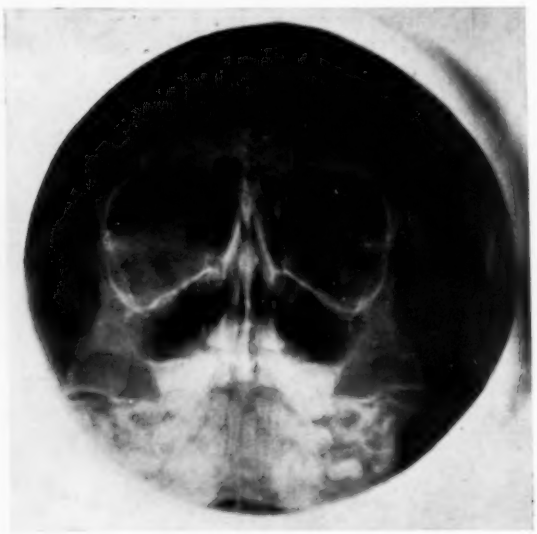

FIG. 1. Normal sinuses, patient six years of age.

FIG. 2. Normal sinuses, adult.

* Read at the Thirty-first Annual Meeting, American Roentgen Ray Society, West Baden, Ind., Sept. 23–26, 1930.

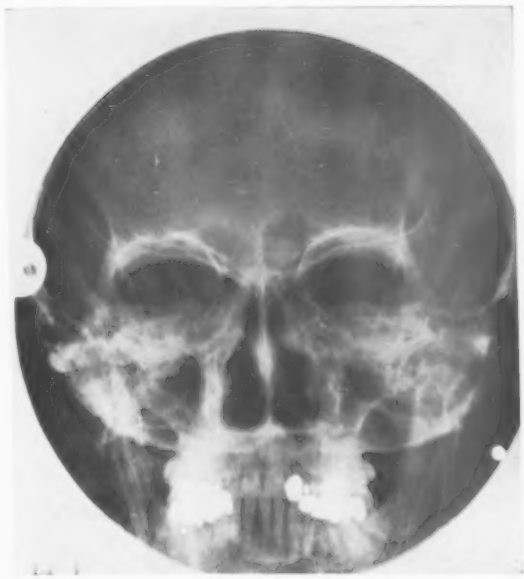

Fig. 3. Osseous growth in the frontal sinus, usually of no clinical significance.

Fig. 4. Foreign body in the antrum (gauze). Post-operative re-examination because antrum continued to drain.

evidenced by a generalized increased bone density which is very irregular or fuzzy in appearance. There is always a pansinusitis, and the same characteristic changes as observed in the sinuses are seen in the nose.

The anatomical or developmental variations of the frontal sinuses are very pronounced. The frontal sinuses vary greatly in shape and size. There are no material variations of the ethmoidal sinuses. The antra are virtually uniform and present fewer variations than any other of the nasal sinuses.

The tissues of the nasal sinuses cast

Fig. 5. All sinuses on the right normal; pansinusitis left.

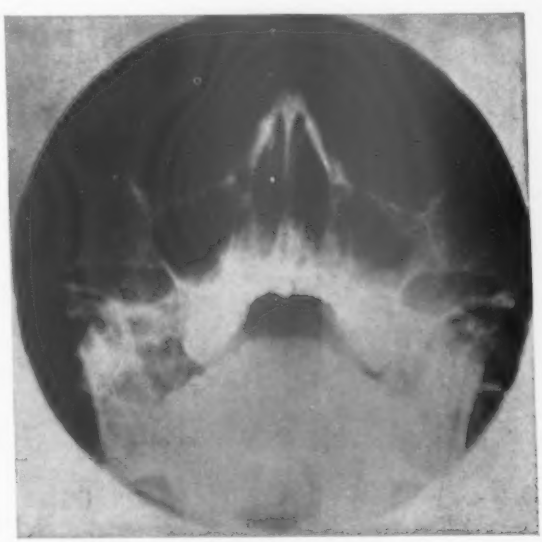

Fig. 6. Right antrum normal; clean-cut multiple polypi left.

Fig. 7. Sinusitis with pus in the right antrum; chronic hyperplastic membrane left.

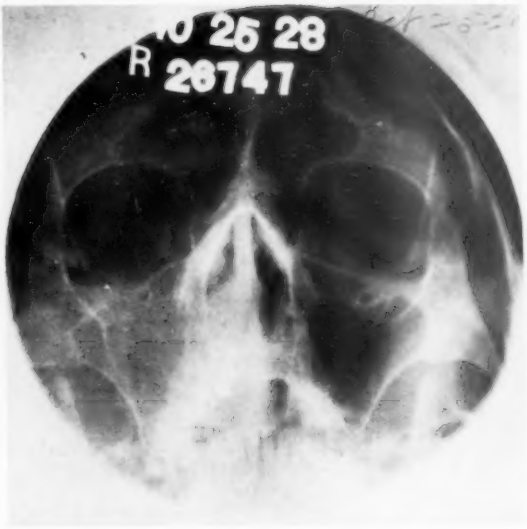

Fig. 9. Malignancy right antrum. Note uniform increased density of the nasal septum.

their shadows on the roentgenograms and vary from the normal as an increased or decreased density. The majority of the pathological lesions, therefore, differ as to density and contour and thus present individual characteristics.

In the roentgenogram of a normal sinus there are no shadows; if there are shadows, varying from the normal anatomical sinus, these shadows are anomalous or pathological.

Further circumspect studies of these shadows will frequently enable the roentgenologist to report the exact pathological anatomy and thus further assist the rhinologist in the best method of treatment for the restoration of the sinus to normal.

Fig. 8. Sinusitis right frontal, left ethmoid and left antrum. The left frontal, right ethmoid and right antrum are normal.

Fig. 10. Chronic sinusitis in the antra, patient nine years of age with pulmonary inflammatory reaction (see Fig. 11).

Fig. 11. Roentgenogram of the chest of same case as shown in Figure 10. See sinuses in Figure 10.

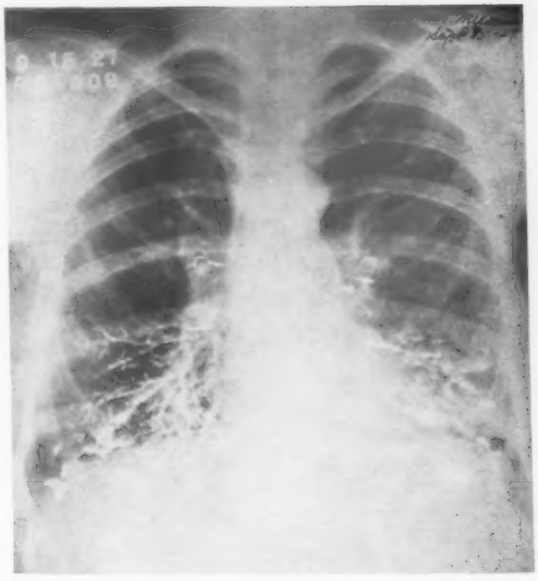

Fig. 13. Roentgenogram of the chest of same case as shown in Figure 12.

The differential diagnosis of the various pathological changes of the sinuses is, in a number of instances, essential. There are other lesions in which the differentiation is not of material value. The acute empyema of the frontals, ethmoids, and especially the antra, as the antra are more frequently involved than all of the other sinuses, is very characteristic and may easily be differentiated from other types. The differentation between a hemorrhagic sinus and a pus sinus may not be made from the roentgen examination alone. The history of a trauma will aid in the diagnosis. The allergic membrane

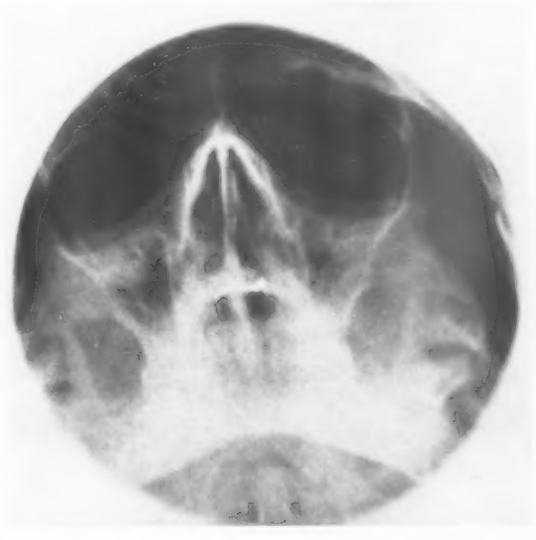

Fig. 12. Chronic sinusitis of the right and left antrum; adult with a well-marked bronchiectasis of the base of the right and left lung (see Fig. 13).

Fig. 14. Chronic sinusitis with polyp formation in an adult with extensive bronchiectasis of the left lung (see Fig. 15).

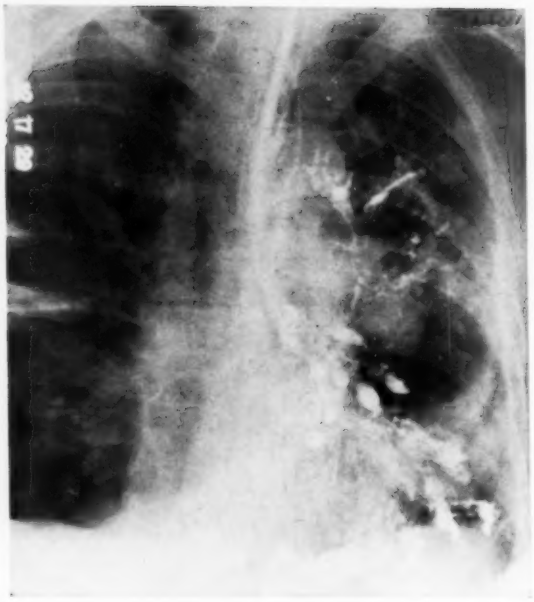

Fig. 15. Roentgenogram of the chest of same case as shown in Figure 14.

may be differentiated by an analysis of the nasal secretions which contain eosinophiles in 70 per cent of allergic individuals as contrasted with 9 per cent in non-allergic patients.

The differentiation of a polyp, mucocele or cyst is difficult and is of little value, inasmuch as the same operative procedure must be employed in each instance. Multiple polypi and hyperplasia of the lining may be differentiated but is again of little significance. The chronicity of a sinus involvement is usually well established by the characteristic increased bone density.

The roentgen ray properly applied always reveals the existing anatomical and pathological status of the tissues of the nasal sinuses, but is of value only in direct proportion to the ability of the roentgenologist to make the correct interpretation.

The fundamental principles in the interpretation of sinus roentgenograms was well covered by Grier[1] in a recent paper. He states that a lack of knowledge of sinus pathology as demonstrated by roentgenographic changes is the real stumbling block in the progress of interpreting sinus pathology, and that the difficulties are increased because the roentgenologist and rhinolo-

[1] Grier, G. W. The interpretation of sinus roentgenograms. Am. J. Roentgenol. & Rad. Therapy, 1930, *24*, 21–28.

Fig. 16. Sinusitis with hyperplastic membrane of the left antrum with a large clean-cut polyp in the right antrum, following the injection of lipiodol in the right and left antrum; the right antrum is completely empty, there is a trace of the oil in the left.

Fig. 17. Same patient as in Figure 16, with the right and left antrum filled with lipiodol. The hyperplastic tissue is evident in the left antrum, the polyp in the right antrum is completely obscured by the lipiodol (see Fig. 16).

gist do not understand one another, even when they attempt to cooperate.

It seems to me that the best way for the roentgenologist to become competent to make dependable readings of roentgenograms in these sinus cases, is to have many opportunities of observing directly the pathological sinus at the time of operation. During my eleven years with Dr. Dean in the University of Iowa, I was afforded an excellent opportunity to observe many operative procedures and findings, after having made a thorough study and report of the roentgen findings. This cooperation thoroughly convinced me that the difficulty between the roentgenologist and the rhinologist, in the majority of cases, is not the fault of the roentgenologist but is the result of the manner in which the rhinologist visualizes his surgery or the existing pathological lesions present.

It is known that there has been much disagreement and misunderstanding between the roentgenologists and the specialists in diseases of the head over the roentgen reports and the operative findings of the surgeons.

Roentgenologists are familiar with the various reasons for the discrepancies or differences of opinion in the roentgenologist's report and the findings of the rhinologist at operation. (Again it may be said that the report of the roentgenologist as to the existing pathology is in all probability correct.) The rhinologist often reports negative findings, but the rhinologist's report of a gross discrepancy between his

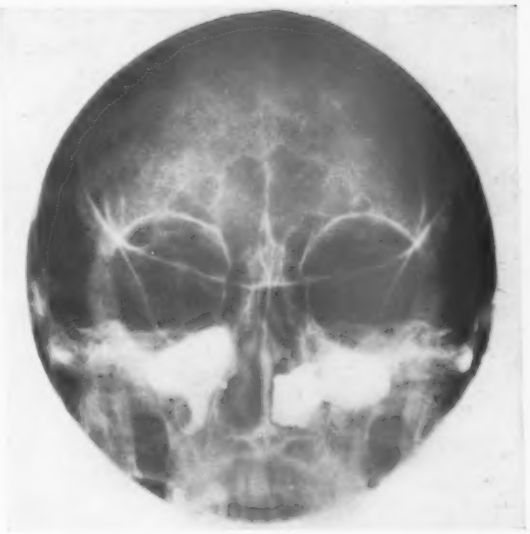

Fig. 19. Shows pathology in the right and left antrum more distinctly than before the injection of lipiodol (see Fig. 18).

Fig. 18. Chronic sinusitis left antrum; chronic sinusitis of the right antrum with a large polyp formation (see Fig. 19).

Fig. 20. Sinusitis of the left antrum. See Figure 21 after operation.

findings and the roentgenologist's report is of value only according to the method of his operative procedure. Obviously the opinion, or the negative findings reported

Fig. 21. Showing result of operation (see Fig. 20).

by the surgeon using the nasal route should not disprove a positive roentgenographic finding, since the surgeon is working indirectly, in the dark, and is obviously unable to visualize the condition of the tissue, and therefore, is in no position to discredit the roentgenogram.

Dscussion on Papers by Beeler, Smith and Collins, and Allen

Dr. J. Brown Farrior, Tampa, Fla. In a study of both the primary and the lipiodol films that were shown by the first essayist, there is not a roentgenologist who cannot interpret primary films even to the degree of an acute or chronic condition and in most instances to the extent of thickened membrane, polyp or cyst and, frequently, the very location and amount of pathology. This is plain to me without the lipiodol. The use of lipiodol means more manipulation and frequent reactions, all of which should be reduced to a minimum in the handling of any condition of our patients. In discussing Dr. Allen's paper, if chronicity is established there is but one way and that is to open the sinus and remove the pathology. Therefore, I have held that with the class of x-rays I have had a chance to observe and with the reports that I get, that manipulation is not necessary. In some cases it may be a more definite proof to the patient, but the chronicity cannot be any more established than you have acquired from the clinical history and the x-ray. Consequently I believe that many of you will live to see this enthusiastic move in the use of lipiodol subside and take its place beside bismuth injection of the antra in chronic maxillary sinusitis.

Dr. R. C. Beeler, Indianapolis, Ind. Dr. Allen's paper has covered the subject up to the use of opaque oils in nasal sinuses. And after hearing his paper I am more inclined to think that the use of opaque oils will carry on this work and give us still more aid in diagnosis. All of us have had difficulty in convincing the nasal specialists of some of our findings. And if we deliver the result to the patient the rhinologist must use and regard our findings. Dr. Allen has shown a slide of a maxillary antrum injected with oil, and he showed you that the polyp was abscured by the density of the opaque oil. He did not show you a lateral view of this same case. If he had, we should have seen the size and position of the polyp. It is very necessary to get the two views in each case. This type of lesion we have found is often the cause of much trouble because large amounts of pus may be held within the cyst. It is necessary to remove pathology of this sort for the patient to recover.

The best position in this work has yet to be worked out. We believe that the positions, posteroanterior and lateral taken with the patient in the erect, are best. The pathology is more often found on the base of the maxillary sinus. We do not know whether we are ready to say that the Potter-Bucky diaphragm should be used. Most of our films have been made without it. The better the contrast between the opaque oil and the muco-periosteum, the more pathology we may show. Speed, however, is a factor because movement during the exposure may lead to a false diagnosis. The patient is usually uncomfortable because of the oil running into his throat, and of course more apt to move.

Simple apparatus can be constructed with a sinus board attached and the angle obtained by movement of the tube. Some of our best films have been taken with the central ray directed parallel to the base of the maxillary sinus.

The sinus should be filled with the oil until it is seen to spill over through the normal ostium. In some cases the displacement method of Proetz and Ernst may be of value. This is especially useful in the study of the sphenoids and the smaller cells. Dr. Farrior says he can read these sinuses without injecting them with oil but can we as roentgenologists feel sure of ourselves in every case? Is it not better to use the opaque oils in those cases where there is doubt? We do not use this method as a routine but in selected cases. We are finding, however, that it has shown more actual pathology than the primary film has indicated.

In closing, I would say that I believe the use of opaque oil in the diagnosis of maxillary sinus disease has come to stay and that the roentgenologist will get far more credit than he has in the past if he will add it to his examinations of these special cases.

Dr. George W. Grier, Pittsburgh, Pa. I want to take another opportunity to emphasize the absolute necessity of the finest technique, the finest films possible if you are going to make accurate diagnoses of sinus disease. Possibly everybody in this room knows that. It won't do any harm to emphasize it again. It is impossible to make an accurate diagnosis unless your film is the very best. It must show all of the septa between the ethmoid cells, for instance, in order for one to make a differential diagnosis of sinus disease. The patient has to be in the proper position. He ought to have several projections. Personally, I prefer stereoscopic plates. That is a personal matter, but I am satisfied you can get more information by studying stereoscopic plates. Certainly a superior inferior view is indispensable.

If you have plates of this quality and study them properly, there are certain things about which I feel there will be little argument. For instance, in empyema of the sinuses, there is very seldom any doubt about sinuses filled with pus—frontals, ethmoids, sphenoids or antrum. If they are filled with pus, if you have well-made plates, the diagnosis is usually obvious.

There are only two or three things that can give the same appearance, sinuses filled with polyps, sinuses filled with new growths, perhaps syphilis. All these others are easily ruled out. So empyema should give very little trouble. The other chronic hyperplastic conditions should give little trouble—thickened mucous membrane, polyps, mucocele, and cysts. These should be easily recognized if you have films of the proper quality. Personally, I don't believe there is any room for argument about lipiodol, in the antrum particularly. It certainly often adds to the sureness of the diagnosis. I am not qualified to state whether the procedure does harm or not. It is certainly a valuable diagnostic aid.

These things I have mentioned can usually be seen in the plate primarily without injection. The only things that remain then in which there is room for debate, and this is the field in which there is always going to be some question, it seems to me, are the cases of chronic sinusitis. One must remember that the cases of chronic sinusitis are not stationary, that they have periods in which the physical condition is different. I have two girls working in my office who are subject to chronic sinusitis. Occasionally you can x-ray one of those girls and find the antrum filled with pus, and I have seen other times when you couldn't see anything. It is obvious that it depends on when this case of chronic sinusitis is roentgenographed as to what the findings will be. The rhinologist must remember that. The roentgenologist is not supernatural and if we happen to get a case of chronic sinusitis in an interval in which there is very little inflammation and no particular thickening of the membrane, the roentgenogram will be negative. If you get it in a period when it is filled with pus, there will be an entirely different situation.

In general, there are two appearances in this kind of a case which give me a great deal of trouble. There are cases in which there is obviously a slight thickening of the membrane. I admit I can't tell whether the thickening of the membrane has any significance at all or not. I don't know whether this patient has had a sinusitis after influenza fifteen years ago, from which he recovered and he has had no trouble since, or whether he has a slight chronic inflammation there that flares up once in a while and may be inactive at that time. I don't believe anybody can tell from the roentgen examination alone.

Then there are the chronic cases of sinusitis in which there is not a definite, real thick, dense membrane. In those cases, there is a general opacity of the sinus. It is very difficult to tell whether that is due to a thickened edematous membrane or perhaps a little pus collected there. These are the cases in which the rhin-

ologist should be able to make the diagnosis by clinical methods.

Dr. Collins (closing). I hope that we haven't left the impression that we think lipiodol should be injected into every sinus. In fact, lipiodol is injected many times by the rhinologists when we think it isn't necessary. Ofttimes they are not willing to accept the word of the roentgenologist. I suppose that any time a paper is read on the subject of lipiodol in the antrum or other sinuses there will be room for discussion on both sides. I think it was obvious in many of the slides we showed that lipiodol injection was not necessary for the diagnosis and we only put it in to corroborate our previous findings. We insist on having preliminary films in every case before the oil is injected.

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ANOMALIES IN TOPOGRAPHY OF THE ALIMENTARY TRACT*

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THE visceral topography of the living normal subject is shown by the roentgen ray to differ from the conceptions laid down in the standard textbooks of descriptive anatomy. These differences are variations which evolve from adjustments in the

FIG. 1. Example 1 shows by a roentgenogram of an opaque enema the non-rotation of the colon. The cecum lies in the middle of the pelvis and the ascending colon lies slightly to the left of the vertebrae. The small intestine fills the right abdomen as shown by the increased intestinal gas in that area. A group of opaque gallstones may be noted in the right upper abdomen (see Fig. 2).

disposition of the viscera to the bodily habitus of the individual.[6] Although they create different topographical pictures, there is essentially a conformity to the norm of general relationships, which result from the dynamics of embryological development. The perversion or the arrest of the dynamics of development create other, truly abnormal, variations in topographical anatomy, many of which carry through with a normal functional status into the adult postnatal life of the individual. Those which are so gross as to result in intrauterine or early postnatal death form no part

FIG. 2. Example 1 shows by a roentgenogram of an opaque meal how the duodenum joins the jejunum in the right abdomen, and these, with the ileum, lie altogether in the right abdomen, at the right of the vertebrae and the colon.

of this presentation. The variations, of which roentgenograms are presented, result by departures from the normal sequence of the very late movements of embryonic development. These may be considered as trivial when compared with other gross errors which entirely pervert the so-

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Fig. 3. Example II shows, by a roentgenogram of a double opaque meal, the stomach lying well to the left of the vertebrae with the duodenum joining the jejunum at the right of the vertebrae. The small intestine lies wholly in the right portion of the abdomen and the pelvis. The barium-filled colon is seen extending from the middle of the pelvis upwards and along the midline and into the left abdomen.

matic development into anatomical monstrosities, and produce non-functioning results. But these lesser departures from the normal present themselves to the roentgenologist and often must be recognized as more than merely interesting anatomical exhibits. The interpretations of the roentgenograms are based upon the manner of the final developmental movements of the embryonic intestinal tract.

The anomalies which present themselves in adult life are chiefly those of the midgut. Two reasons for this may be suggested: first, the individual is short-lived if the aberrent development is so extensive as to involve the foregut or the hindgut, or both, i . any manner other than in position (Fig. 10); and second, the midgut has a much more extensive movement due to its greater elongation and its migration back through the umbilical orifice from the umbilical celom into the abdomen, where its complicated disposition is fixed by peritoneal fusions.

The early elongation of the midgut causes it to form a loop opposite the attachment of the yolk stalk and then to assume a lateral twist so that the cephalic limb of the loops falls to the right and the caudal limb to the left. This movement is probably related to the lefthanded (clockwise) helical direction of histogenesis of the gut.[4] Con-

Fig. 4. Example III shows, by a roentgenogram of a double opaque meal, the stomach and the colon in the usual position without evidence of the segregation of the small intestinal loops and of the colon into the right and left abdomen respectively. Figure 5 gives evidence of anomalous rotation, not a simple non-rotation. Reversed rotation may have occurred in this instance but there is no evidence of the duodenum passing ventral to the colon.

tinued growth results in a protrusion of the intestine into the umbilical celom. This extra-abdominal loop is the anlage of the small intestine (other than the duodenum) and of the right segments of the large intestine (cecum, appendix, ascending colon and proximal transverse colon). The movement which returns this portion of the gut to the abdomen is the resultant of the continued growth (elongation) of the intestine and of the lessening of the cavity of the umbilical celom. The small intestine lengthens much more rapidly than does the large intestine. The increasing mass of intestines is transferred from the diminishing umbilical celom into the enlarging abdominal celom. The lengthening small intestine worms into the abdomen dorsal to the superior mesenteric artery and colon, and passes into the left abdomen. The more slowly growing (elongating) right colon also gradually passes into the abdomen until finally only the cecum remains outside. This migration accentuates the axial rotation of the gut as well as the mass rotation of the mesentery and its intestines. This latter result may be thought of as a partial physiological volvulus. When the fusion of the mesentery of the colon to the parietal peritoneum fails, an obstructive volvulus may be superimposed by a pathological twisting of the intestinal mass.[2]

Fig. 5. Example III shows, by a roentgenogram of an opaque meal, the duodenum making a reversed curve and extending to the right of the vertebrae. The observations do not determine if this may be a reversed rotation.

Fig. 6. Example IV shows, by a roentgenogram of an opaque enema, the right colon lying along and to the left of the vertebrae with the small intestinal loops, which were filled through the incompetent ileocecal valve, extending into the right abdomen. Figure 7 shows the duodenum and the small intestine of the same example.

The cecum returns to the abdomen last, terminating the physiological reduction of the embryonic umbilical hernia. It therefore assumes a position above (cephalad) and to the right of the small intestine. The

subsequent elongation of the large intestine continues until the fourth postnatal month and pushes the cecum toward or into the right iliac fossa (Figs. 11 and 12).

Jordan and Kindred[4] list twelve major anomalies of faulty development in the digestive tract—split tongue, harelip, atretic esophagus, local atresias more especially in the duodenum, absence of the gall-bladder, Meckel's diverticulum, perforated diaphragm, situs inversus, brachial fistula, thyroglossal cyst, agnathus and congenital rectocele. Of these only the perforated diaphragm and the varieties of situs inversus including the anomalies of rotation, and perhaps the rare absence of the diaphragm, are subject to discovery by the gastrointestinal roentgenologist. These variations are of large anatomical interest; they create anomalous and puzzling findings in physical diagnosis, complicate surgical procedures unless fully elucidated beforehand, and they are the foundation for malfunction, and for an acute interruption of function by volvulus and other obstruction.

FIG. 8. Example V shows, by a roentgenogram of an opaque meal, the small intestine wholly in the right abdomen, and the cecum and ascending colon lying in the pelvis and in the midline over the sacral promontory. The hepatic flexure approaches its usual position.

FIG. 7. Example IV shows, by a roentgenogram of an opaque meal in the same example as Figure 6, how the duodenum extends to the right of the vertebrae where it joins the jejunum.

Complete visceral transposition is very infrequently seen—in only two instances among over ten thousand gastrointestinal roentgenological studies in the author's experience. The anomalous rotation of the intestine is almost as rare, less than one-tenth of one per cent. However, the migration of the cecum may vary in extent in a large percentage of individuals in whom the manner of rotation of the midgut has been normal. The dynamics of this migration arise from the growth (elongation) of the colon, which continues after the cecum has returned to the abdomen until the fourth postnatal month. The direction of migration is determined because the cecum is held by its own mesentery in the potential space or groove about the root of the small intestinal mesentery between the mass of the in-

Fig. 9. Example VI shows, by a roentgenogram of an opaque enema, the cecum fixed by precocious peritoneal fusion in the infrahepatic position and the appendix lying above. Final reduction of the cecum and adjacent segments from the umbilical celom before the usual movements were complete left the cecum in a relative position which nullified the directional forces for its usual migration (see text).

testines and the liver above and the parietes laterally. With normally completed rotation, no instance has been seen where the migration has failed to form the hepatic flexure. Beyond this, however, the cecum may be arrested at any point or it may continue until it enters the left pelvis (Figs. 11 and 12). This exaggerated migration of the right colon has been demonstrated in the new-born before the true pelvis has formed.[5] It is to be differentiated from the pelvic position of the cecum in the congenital visceroptosis of the asthenic bodily habitus. It is believed that the extent of this migration, whether arrested in the hypochrondrium or continued into the depth of the true pelvis, is predetermined by the degree of the earlier movements, especially that of the axial rotation of the gut, which is a manifestation of the clockwise spiral direction of histogenesis.

A departure from normal in the sequence by which the umbilical loop returns into the abdomen is the hypothesis which best explains the anomalies of rotation. Variation in size of the umbilical orifice is thought by Dott[2] best to account for the differences in the sequence of return. The cecum should normally return last. Non-rotation happens when it returns to the abdomen first before any of the small intestine. If the cecum, by other untimely reduction of the umbilical hernia, should pass into the abdomen before the small intestine has all left the umbilical celom, it would fail to assume that proper position, which will direct its elongation to

Fig. 10. Example VII shows, by a roentgenogram of an opaque enema, the anomalous fixed position of the descending colon in the midline and of the sigmoid about the right of the promontory of the sacrum. There was no evidence of abnormal rotation. There is a reversed splenic flexure.

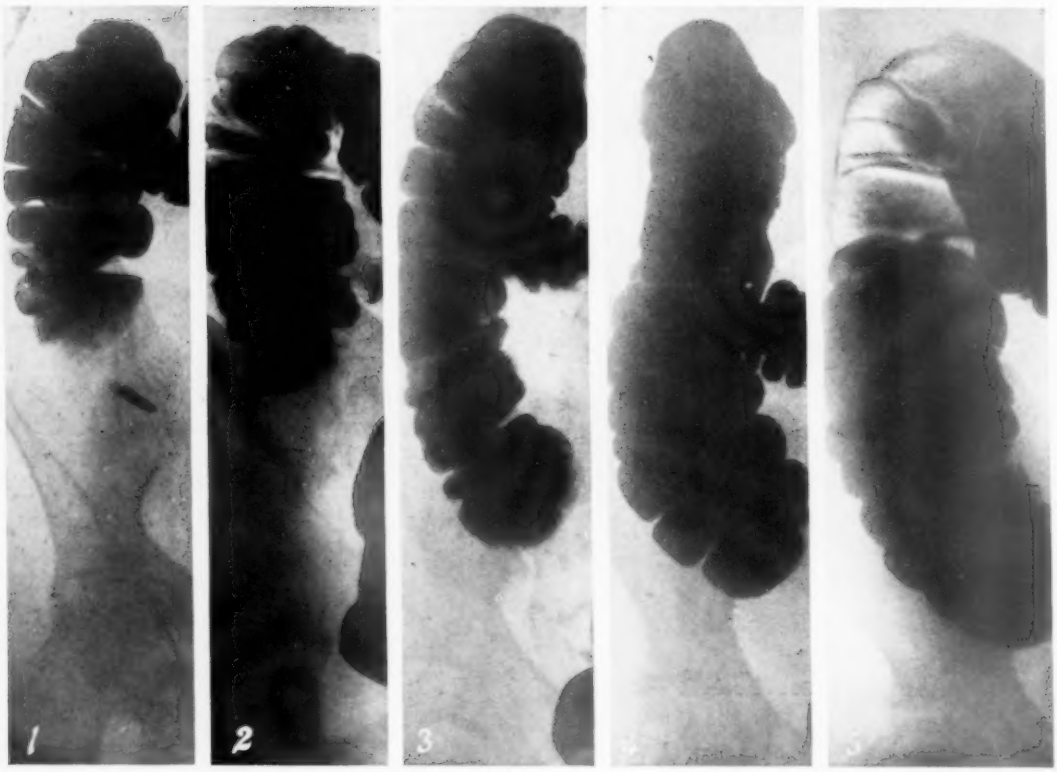

Fig. 11. The descent of the cecum and the ascending colon varies in degree and causes a difference between individuals in the length of the right bowel. The rotation and descent of the cecum may stop at any point below the hepatic flexure. The five examples above, together with the four in Figure 12, illustrate this wide variation.

the right about the root of the mesentery. The inverted subhepatic cecum (Fig. 9) can result when this direction is missed because of precocious return to the abdomen, interrupting the normal reducing movement just prior to its completion. In nonrotation the colon lies in the left of the abminal space and the small intestine lies in the right, infrahepatic portion of the cavity; the duodenum extends to the right and may retain its mesentery; the superior mesenteric artery lies dorsal to the duodenum and there is no crossing of the colon and small intestine. In reversed rotation the small intestine, usually the duodenum, and the superior mesenteric artery cross the transverse colon ventrally. Other less characteristic variations of alimentary topography may occur when the sequence of the return of the umbilical embryonic loop is differently interrupted.

The visceral disposition may be strangely and differently altered by the congenital perforate diaphragm. The abnormal hiatus occurs chiefly in the left diaphragm. The instances, of which roentgenograms are reproduced in this article, indicate that normal rotation has occurred prior to the transfer of any of the abdominal viscera into the left thorax. Whether this transfer occurs as an embryonic migration or as a forcible displacement by the initial respiratory efforts at birth is not clear. It is easily conceived how the various segments of the alimentary tract could be drawn or forced into the thorax by the pressure changes of the first inspiratory efforts. Artificial respiration might even exaggerate the transfer. The action of air pressure is demonstrated at surgical reduction of diaphragmatic hernia, on which occasions a thoracotomy facilitates the displacement and

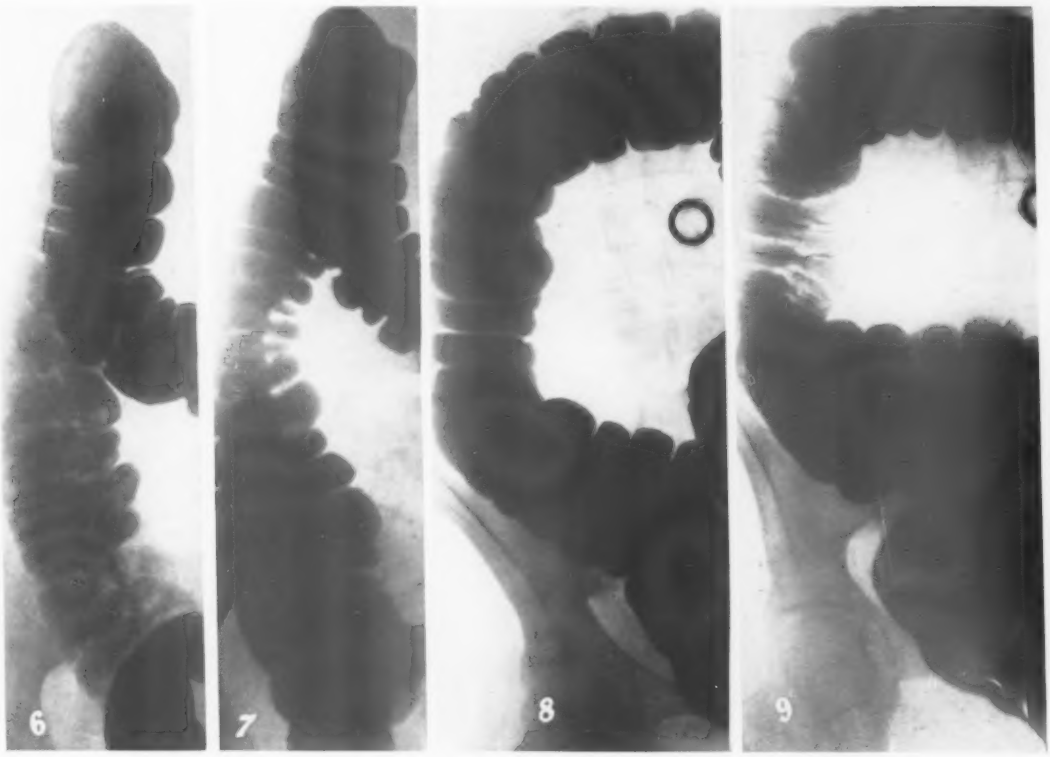

Fig. 12. Four examples further illustrating the variable extent of the descent of the cecum. The pelvic cecum of hyper-rotation differs from the pelvic cecum of congenital visceroptosis in its manner of occurrence and in the length of the bowel proximal to the hepatic flexure. In the last examples, the cecum has folded, otherwise it would have gone into the left pelvis, of which condition examples are infrequently seen.

return of the thoracic abdominal viscera, and lowers the mortality of the operation.

The portions of the tract which enter the thorax follow no rule. In Example VIII, a girl aged six (Figs. 13 and 14), most of the transverse colon and the stomach have passed into the chest. Their combined movement indicates that the posterior wall of the greater omentum and of the transverse mesocolon had already fused. In Example IX, a new-born girl baby (Fig. 15), the entire small intestine, cecum, ascending colon and transverse colon have passed into the chest, leaving the stomach in normal abdominal position. In another example, pictured elsewhere, in a robust young man of twenty-two years, only the cecum and the ascending and transverse colons and the terminal ileum have entered the chest cavity. The stomach retains its normal position and the small intestine is in the abdomen. In these last two examples, there could not have been any fusion of the posterior great omentum and transverse

Fig. 13. Example IX shows lateral and frontal full length vertical roentgenograms of an opaque enema in a child with a congenital perforate diaphragm. The transverse colon is in the left thorax and the cecum and the ascending colon lie transversely in the upper abdomen.

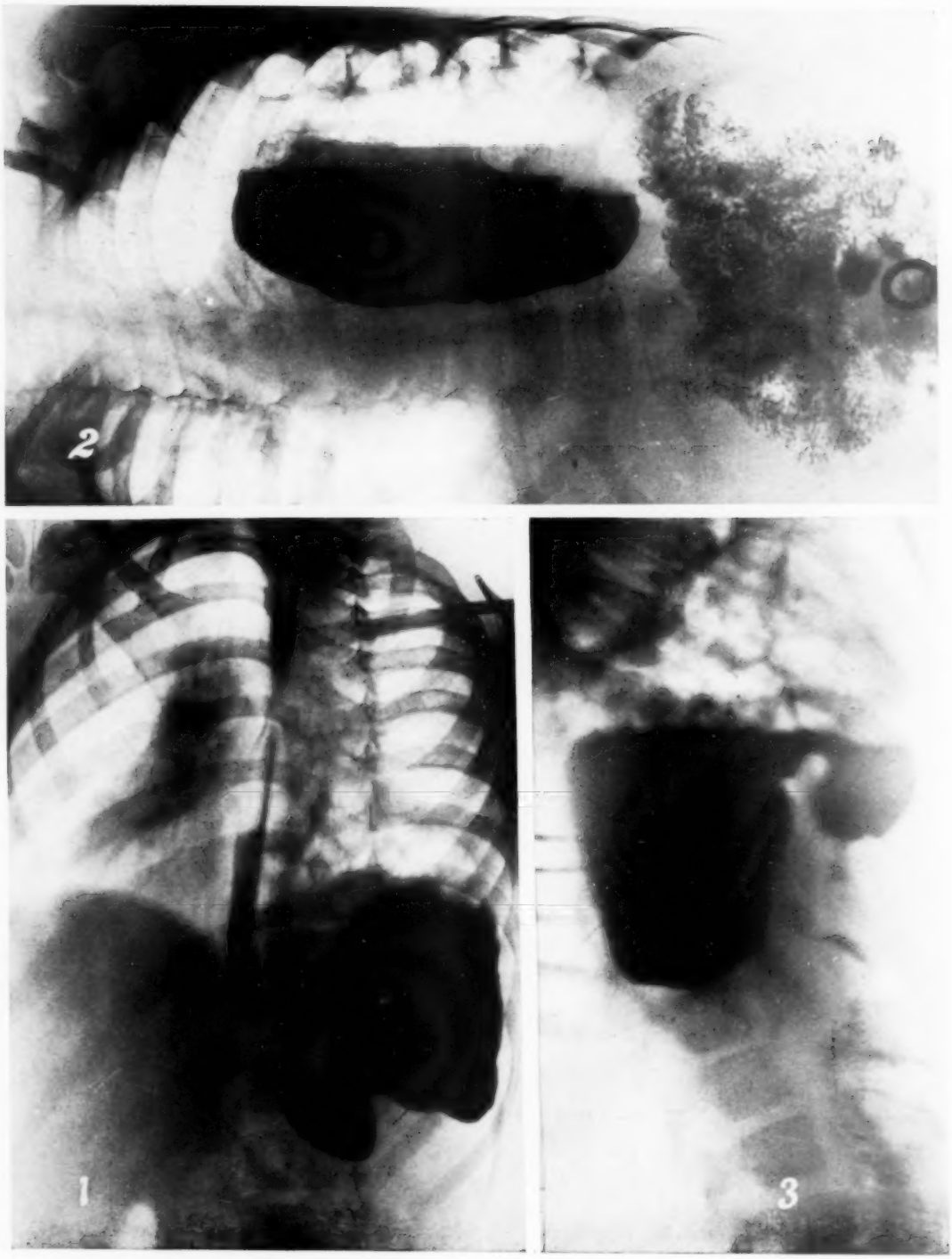

Fig. 14. Example VIII shows, by vertical and recumbent frontal roentgenograms (1) and (2) of an opaque meal, in the same child as Figure 13, the stomach in the left thorax, except for a small juxta-cardiac portion of the fundus. The lateral (3) roentgenogram of the opaque meal, shows the inverted position of the pars pylorica and the duodenum extending downwards to the abdomen.

Fig. 15. Example IX. 1. Shows, by an open non-bariumized picture of a new-born baby, the air-filled stomach in its usual position, and the air-filled small intestine in the left thorax. 2. Shows a roentgenogram of an opaque meal of the same patient. The stomach is in its usual position but the duodenum extends immediately upward into the left thorax. The small intestine is massed in this location. 3. Shows a roentgenogram of an opaque enema with the transverse and proximal colon in the left thorax.

mesocolon. Huntington[3] states that in the embryo at four months the great omentum can still be separated from the mesocolon. Deaver[1] states that their fusion occurs at about the time of birth.

SUMMARY

The roentgenological examination of the alimentary tract encounters infrequently an anomalous topography of the abdominal segments. Several examples of these variations from the normal are presented and the manner of their occurrence discussed. Abnormal rotation is explained by unusual sequence in reduction of the embryonic umbilical hernia. The cecum secures direction to its normal migration by terminating this reducing movement, and its degree of descent is predetermined by the degree of the initial axial rotation of the gut. The variety of the alimentary segments which appear in the left thoracic cavity in instances of perforate diaphragm is partially determined by the state of the fusions of the peritoneum.

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COMPARISON OF INTRAVENOUS AND ORAL CHOLECYSTOGRAPHY*

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THERE is adequate authority in the literature to support the relative advantages of oral and intravenous cholecystography. From the experience of others it is difficult to decide which method to use. Therefore, we have run two series; one intravenous and one oral, comprising in all 500 patients. There was no particular selection of patients for either series. They were all routine cases referred for roentgen examination. Practically all had some findings suggesting cholecystitis. There was no discrimination in choosing which patient would be examined orally and which intravenously.

PROCEDURE IN THE ORAL SERIES

A preliminary film of the gall-bladder area was made the day before the cholecystographic examination. At 5:30 P.M. on the evening of giving the dye, a special supper consisting of eggs, bacon, toast, and custard with cream was given. The dye was taken at 9:00 P.M. Following this no food or water was allowed. Films were made at twelve and fourteen and a half hours. A second fat meal was then given and an examination for emptying made two hours later.

In this series of 500 cases, gallstones were definitely seen before the administration of the dye in only 8 instances. Therefore, we feel that the preliminary film is not of great value and have discontinued making it. The fat meals were found to cause considerable gastric distress, especially in those cases showing diseased gall-bladders. Because of this fact, and also because it was felt that there might be some delay in emptying of the stomach burdened with the fat meal, and therefore some interference with proper absorption of the dye, the preliminary fat meal was discontinued. One-half of the oral series had a preliminary fat meal, and one-half had an ordinary supper. No difference was noted in the accuracy of the test nor in the clearness or intensity of shadows in normal cases.

We have also observed that unless stone shadows are visualized the gall-bladder always empties. Therefore, we feel that the second fat meal, and examination for emptying, is unnecessary in a patient who shows a normal filling and concentration.

The dye was given in three forms: keratinized capsules, plain capsules and in emulsion. There was no appreciable difference in the density of the shadows no matter in what form it was administered. While an accurate record of the prevalence of nausea, vomiting and diarrhea was not kept, it is obvious that the emulsion was better tolerated. Diarrhea of sufficient intensity to make the absence of shadow of questionable value was rare. When the diarrhea was marked and the gall-bladder cast no shadow the examination was repeated and two drams of paregoric given with the dye.

PROCEDURE IN THE INTRAVENOUS SERIES

A fat meal was given the evening before administration of the dye. No laxative was allowed on the day before. The dye was given at 8:00 A.M. and films made four and six hours later. If no shadow, or only a faint shadow, was seen at six hours another film was made at eight hours. A fat meal was again given and a final examination for emptying made two hours later.

There was only one serious reaction in this series. That was in an elderly patient with advanced arteriosclerosis. The patient became severely shocked and for about four hours there was doubt about his recovery—but he recovered. There was a mild reaction in all the patients. There were

* From the Radiological Department of the George F. Geisinger Memorial Hospital, Danville, Pa. Presented before the Philadelphia Roentgen Ray Society, Nov. 6, 1930.

no serious difficulties locally at the site of injection.

We have avoided giving the dye, in any form, to patients having symptoms of acute cholecystitis. The dye aggravates the symptoms to such an extent that we do not believe the information gained is worth the suffering.

Twenty-five of the intravenous series were done with iso-iodeikon. There seems to be no question that this form of the salt produces less reaction. None of the 25 had any untoward symptoms. The shadows in the normal cases were much more dense. There was not a little difficulty in making accurate readings in comparing the serum color with the standards. This series is, however, too small to warrant a statement concerning the liver function aspect of the test.

The statistics of the two series are given in Table I. The ratio of normal to diseased is similar in both, the intravenous showing

Table I

	Oral	Intravenous
Total	265	235
Normal	117	119
Diseased	135	107
Inconclusive	13	9
Operated upon	78	68
Proved errors	8	6
Normals, confirmed at operation	6	9

a slightly higher ratio of normals. The difference is not great enough to be of significance.

The 13 inconclusive cases in the oral series were due to two causes: first, failure of adequate absorption of the dye and second, technical difficulties, particularly motion on the part of the patient. The number of inconclusives in the oral series is larger but the difference is not great.

The percentages of proved errors in the two series are: 9 per cent in the intravenous and 10 per cent in the oral. These percentages are not as absolute as the figures indicate as, I hope to show in discussing the errors.

The last items in the table are cases which were operated upon for some other cause than cholecystitis and the finding of a normal gall-bladder by roentgen examination confirmed.

Oral Errors

The findings in the cases in error will repay a little study. In Table II are tabulated the findings in the cases in error in the

Table II

Oral Errors

Reported Normal—Found Diseased

1. Strawberry gall-bladder
2. Fibrosis of gall-bladder

Reported Diseased—Found Normal

3. Normal gall-bladder—necrotic areas in liver.
4. Cirrhosis of liver
5. Acute appendicitis
6. Duodenal ulcer
7. Duodenal ulcer
8. Duodenal ulcer

oral series. The first two were reported normal and were found at operation to have diseased gall-bladders. This is a natural error of the test. A certain percentage of these errors is to be expected, for some diseased gall-bladders will retain enough function to cast a normal shadow.

Reported Diseased: Found Grossly Normal at Operation: The liver in this patient was found to be studded with a number of areas of necrosis. The amount of liver tissue was by no means half destroyed and there should have been enough normal tissue present to give an adequate excretion of the dye. This gall-bladder was not removed so it is possible that there was alteration in the gall-bladder sufficient to cause failure to concentrate. In one patient in this series the cholecystogram indicated a diseased gall-bladder and at operation it was grossly normal. It was removed, however, and found on section to be densely infiltrated with small round cells and a few leucocytes. This indicates that the gross appearance of the gall-bladder is not always an indication of its normality. Before an error in cholecystography is finally admitted the gall-bladder should be examined microscopically.

No Shadow Cast: Gall-Bladder Normal: At autopsy this patient showed an ad-

vanced cirrhosis of the liver. This adequately explains the failure of the shadow to appear. This gall-bladder was normal microscopically.

No Shadow: Normal Gall-Bladder: Acute Appendicitis: It is well established that acute disease elsewhere in the abdomen will prevent a normal gall-bladder from properly functioning in cholecystography. Gall-bladder not examined microscopically.

No Shadow—Duodenal Ulcer: Three patients had duodenal ulcer and a grossly normal gall-bladder which did not cast a shadow. In 2 cases the diagnosis of ulcer was made before operation. The gall-bladders were not removed from any of these patients.

INTRAVENOUS ERRORS

The findings in the cases in error in the intravenous series are given in Table III.

TABLE III

Intravenous Errors

All reported Diseased

1. Normal
2. Normal
3. Hydronephrosis
4. Adhesions to cecum and colon
5. Appendicitis
6. Duodenal ulcer

The first two were reported diseased and were found to be normal. Both had poor histories of gall-bladder disease. The operation was performed on the evidence of the intravenous cholecystogram.

No Shadow: Hydronephrosis: The preliminary film showed several small dense shadows scattered about the right upper quadrant over a large area. Repeated films showed them in widely varying positions. No shadow appeared on the cholecystogram, hence they were thought to be stones in a greatly distended gall-bladder. An enormous hydronephrosis, having a volume of about a quart was found which pressed against the under surface of the liver and perhaps thus prevented the gall-bladder from filling. The gall-bladder was not removed.

No Shadow: Adhesions to Cecum and Colon: This patient had many dense adhesions to the cecum and transverse colon. These might have caused the symptoms but they would scarcely prevent the gall-bladder from filling. Gall-bladder not removed.

No Shadow: Appendicitis: This patient did not have a frankly acute appendicitis, but there was a definite inflammation present, more than one would call a "chronic" appendicitis. No microscopic section of the gall-bladder.

No Shadow: Duodenal Ulcer: Again duodenal ulcer appears associated with a grossly normal gall-bladder which failed to cast a shadow. Gall-bladder not removed.

DISCUSSION

The absolute percentage of accuracy of the two series is difficult, almost impossible, to determine because there are so many extenuating circumstances. Of the 14 cases in which the gall-bladder was grossly normal, it was removed and examined microscopically in only 3 instances. That leaves the remaining 11 with some doubt as to whether or not they were definitely normal gall-bladders. In the oral series there was in each instance some finding which could account for the failure of the shadow to appear. Three of these had duodenal ulcer. As none of these gall-bladders were examined microscopically, it is possible that there was an associated cholecystitis. Many patients with duodenal ulcer will of course show normal gall-bladder shadows.

The record of the intravenous errors is not as good. Here 2 out of the 6 errors had no other pathological findings to account for the failure of the shadow to appear. Six of the 8 oral errors were benefited by the operation; although the preoperative diagnosis was incorrect, no unnecessary operation was done. In the intravenous series, however, 3 of the 6 were unnecessarily operated upon because of cholecystographic errors. This higher error in the intravenous series was due, for the most part, to the placing of too great faith in the in-

travenous method, and not giving the history sufficient weight. It is not always necessary, but usually advisable, to have the history and roentgen findings in agreement.

We were surprised to find the accuracy of the two series so close. Before running this comparison of the methods, we felt that the intravenous was much more accurate, and frequently repeated oral examinations by the intravenous method. Confidence in the oral method is now raised to a level as high as that formerly enjoyed by the intravenous; intravenous examinations, for purposes of checking the oral method are no longer done.

CONCLUSIONS

The oral method of cholecystography is preferred because:

1. It is easier on the patient mentally. He does not, with the oral, have the unpleasantness (and in some cases terrors) of venipuncture.

2. There are fewer reactions.

3. The oral reactions are not as severe.

4. It is a simpler method in routine procedure.

5. For practical purposes it has proved as accurate as the intravenous.

THE TREATMENT OF MELANOTIC TUMORS OF THE SKIN: PIGMENTED MOLES AND MALIGNANT MELANOMAS*

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DETROIT, MICHIGAN

PIGMENTIFEROUS formations of the skin are of two main groups. First, the pigmented mole (nevus pigmentosus), a benign or harmless lesion, usually flat or wart-like, or occasionally a papillary excrescence, and, second, the malignant melanoma (melanosarcoma), the most dangerous of all neoplasms afflicting the human body.

A most interesting relation exists between these two processes. It has long been observed that a pigmented mole, when subjected to chronic irritation or repeated trauma, becomes transformed into a malignant melanoma with a rapidly fatal outcome. And contrarywise or conversely, an irritated pigmented nevus with definite clinical signs of a malignant degeneration may spontaneously become quiescent or even undergo regressive atrophic changes.

These facts have a most vital therapeutic bearing, for our agents should be so chosen that the first occurrence will be prevented and the second favored.

We shall endeavor to demonstrate by means of carefully selected cases that many of the therapeutic procedures now in use do not satisfy these requirements—that they are not only valueless but positively harmful. We shall also attempt to suggest the most desirable method to be followed in the treatment of these lesions.

THE INFLUENCE OF DIRECT TRAUMA

The pigmented mole, whether of the congenital or adult type, without interference usually pursues an entirely harmless course. It grows slowly for a long time, then ensues a stage of quiescence or inertia, and terminates in regressive changes such as atrophy and fibrosis. Under the influence of trauma a period of increased activity often develops. The overgrowth of the cells leads to increased size of the mole, the nuclear hyperchromatism and the increased vascularity change the color from brown to purplish and from light black to deep black. Ulceration may result from infection through surface abrasion. Usually these irritative changes regress spontaneously but if the trauma persists a malignant degeneration may follow. Our series includes several such cases and these will be reported briefly.

Case 1. G. W., white, male, aged twenty-six. A pigmented mole had been present since birth on the inner aspect of the upper third of the left leg. On August 21, 1928, this mole was injured by a piece of flying metal. There was bleeding and secondary infection, and retarded healing. On account of persistence of ulceration, wide excision of the lesion was done on September 25, 1928, five weeks after injury. The microscopic report on the removed tissue was cellular fibroma, non-malignant (Figs. 1 and 2).

In December, 1928, there was a local recurrence in the surgical scar. On January 15, 1929, a tumor about 3 cm. in diameter was present and a second wide excision was done. The microscopic report on this tissue was spindle cell histoid melanosarcoma (Figs. 3 and 4).

From February 4 to 7, 1929, the patient was treated extensively with deep roentgen rays.

On April 2, 1929, numerous skin and visceral metastases were observed. One of the skin nodules was removed for biopsy and the microscopic report was again spindle cell histoid melanosarcoma.

On April 29, 1929, the patient died—eight months following injury to a mole that had been quiescent for twenty-six years.

* Read at the Thirty-first Annual Meeting, American Roentgen Ray Society, West Baden, Ind., Sept. 23–26, 1930.

Case II. R. A. F., white male, aged thirty-nine.

In 1926, the patient first noticed a pigmented mole about 1 cm. in diameter, on the left calf. This lesion continued unchanged until October, 1927, and then due to an injury with an indoor baseball bleeding occurred. Healing followed without interruption. During the summer of 1928, slight growth was observed. In September, 1928, an ulceration with secondary infection developed at the site of the mole. At this time, the lesion was removed by electrocautery. The microscopic report was that of melanosarcoma.

Generalized metastases quickly followed with involvement of lymph nodes, skin and lungs.

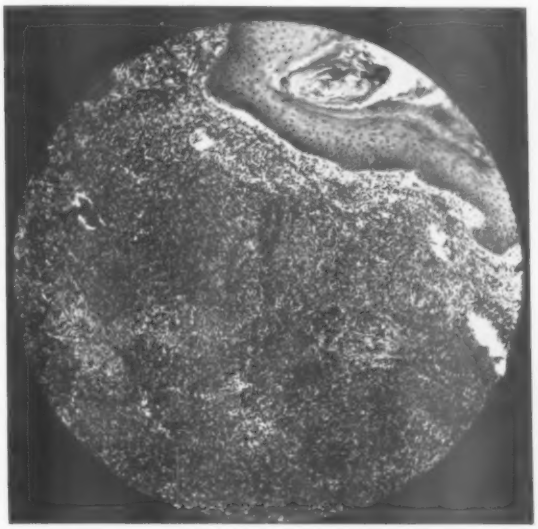

Fig. 1. Microscopic section of Case 1. Low power. Cellular fibroma.

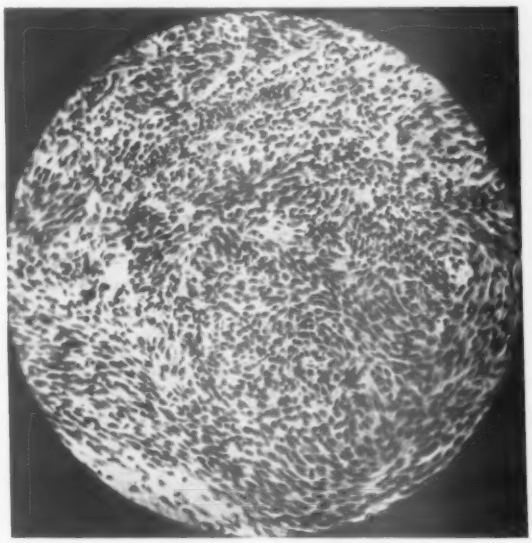

Fig. 2. Same as Figure 1. High power.

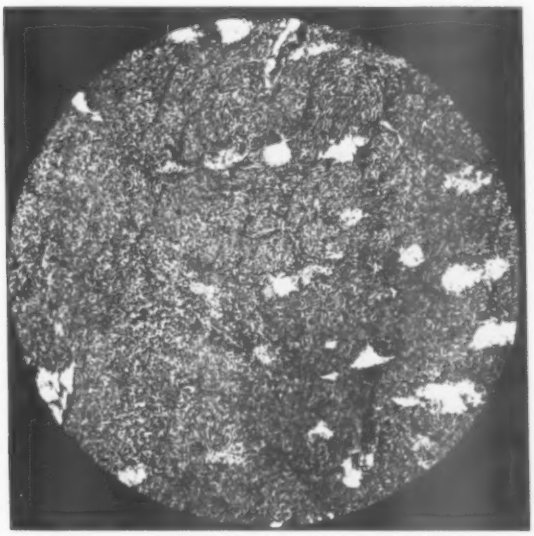

Fig. 3. Same case as Figure 1 four months later, showing transformation into malignancy: spindle cell histoid melanosarcoma. Low power.

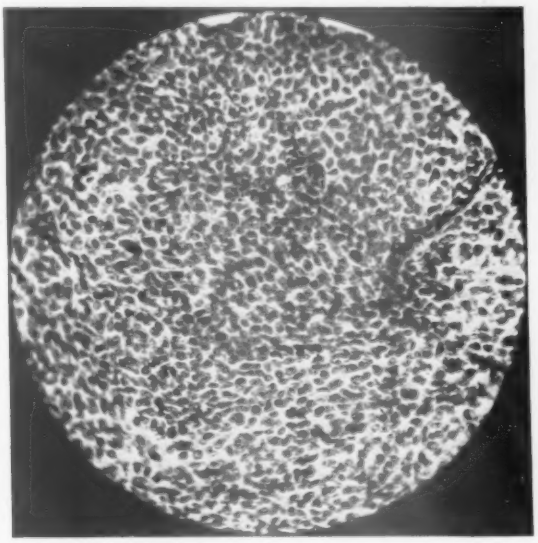

Fig. 4. Same as Figure 3, high power, showing the very malignant character of the cells.

Numerous roentgen treatments were given from October 8, 1929, to October 21, 1929, with only passing benefit, and the patient died on January 2, 1930.

Case III. J. R., white male, aged twenty-eight.

In this case a pigmented mole had been present on the upper third of the inner aspect of the right thigh for several years. In the first week of October, 1929, this lesion was directly injured by the patient falling over a wire. Four days later he noticed a small lump at the site of the mole and a second lump in the right groin. The tumor in the groin developed rapidly and by early December was 10 or 12 cm. in diameter. On December 11, 1929, this groin tumor was removed surgically and the microscopic report on this tissue was melanosarcoma. On December 30, 1929, the original tumor was removed. From January 3 to May 10, 1930, the patient received numerous roentgen treatments for generalized metastases with only temporary improvement. The patient passed from our care in July, with his general condition deteriorating, and on August 10, 1930, died.

Case IV. H. McE., white male, aged forty-one.

In the summer of 1920, this patient struck his left thumb with a hammer. The nail became black and slowly became detached. Within a few months a small tumor developed at the site of injury. This was removed in the summer of 1921, no microscopic study being made.

Late in 1921 and in 1922, the axillary and infraclavicular lymph nodes became involved. These were surgically removed and when sectioned proved to be melanosarcoma. From September, 1922, to April, 1923, the patient was given several series of deep roentgen treatments for the wide-spread lesions but exitus occurred on July 18, 1923.

Case V. C. S., white male, aged thirty-five.

In this case a warty pigmented mole had been present in the left subscapular region since birth. In 1921, the patient believed the mole to be increasing in size. He consulted an osteopath who advised and applied very intensive massage over a period of several months. Under the influence of this treatment, the mole became irritated but upon the discontinuance of these manipulations, its original size was regained.

In December, 1921, several masses appeared in the axilla. These were removed by operation in February, 1922, and microscopic examination showed a very malignant polymorphous celled melanosarcoma.

Generalized metastases developed. On June 6 a tumor mass the size of a small orange was present at the site of the original pigmented mole. Two series of deep roentgen therapy were given in June and July, but the patient died on September 14, 1922.

It is difficult to ignore the preëminent rôle of trauma in the above instances. In Cases I, II and III, a single violent injury resulted in malignant degeneration of moles which apparently were in a quiescent stage, with rapidly fatal termination (the first case dying in eight, the second within fourteen and the third barely surviving ten months). In the fourth case, with injury to the nail fold, which tissue gives rise to melanomas of more benign character, death was postponed for nearly three years; and in the fifth case, where there was repeated trauma by massage to a preëxisting mole, death resulted within fourteen months.

Ewing[10] in a detailed study explains the influence of injuries on the pigmented moles in the following words:

"Through irritation of simple traumatic, or nervous, or more complex origin, the quiescent nevus cells may be incited to overgrowth and renewed pigment production, developing a malignant localized tumor. The overlying epidermis soon participates in this tumor, developing pigment, the presence of which still further stimulates growth and often the extension of the tumor process along the basal cells of previously normal rete pegs. From both of these sources actively proliferating epithelial cells bearing pigment and devoid of fibrils, become disseminated by lymph and blood vessels."

The Influence of Certain Destructive (Traumatic) Therapeutic Procedures

We have concluded that certain destructive therapeutic procedures now employed for the removal of moles or melanotic tumors may act in a similar manner to the above traumas, thus producing degeneration of pigmented nevi into malignant proc-

esses or dissemination of already malignant melanomas to distant parts of the body. Two such methods employed are electrogalvanization and the sparking by high frequency current, both of which, regardless of how carefully applied, act in the form of minute traumatic impulses to the tissues exposed. The same criticism applies to the use of electrocautery and electrocoagulation, if unskilfully used on the pigmented mole or on the tumor formations.

It seems that trauma disturbs the equilibrium which exists between the potentially malignant pigmentiferous cells and the defense mechanism of the surrounding tissues—a phenomenon commonly known as the quiescent state—bringing about a sudden release of malignant tendencies. This leads either to local overgrowth or, more commonly, to extensive secondary spread with rapid lethal outcome.

The following 4 cases are typical of what might and does happen:

Case vi. S. A. M., white male, aged thirty-four.

A pigmented mole about 3 cm. in diameter had been present on the upper sternal region since birth. In April, 1916, the patient noticed that the mole was slowly enlarging and he consulted a physician who applied radium. The dose was unknown, but no erythema resulted. The lesion became quiescent. In November, 1927, the patient consented to its removal, having been influenced by the warning that it might develop into cancer. Removal was effected by electrocoagulation, no microscopic examination being made.

Six weeks following this operation, enlarged lymph nodes were discovered in the right axilla and shortly after in the supraclavicular region.

In September, 1928, he was referred for deep roentgen therapy. Examination at this time revealed a scar about 4 cm. long at the site of the original lesion without evidence of local recurrence. The axillary and supraclavicular nodes on the right side were from 1 to 5 cm. in diameter. From September 18 to November 16, 1928, the patient was given two series of deep roentgen-ray treatments, without permanent benefit, for new metastases appeared and the patient succumbed on June 16, 1929 (eighteen months).

Case vii. M. W. C., female, white, aged seventy-two.

This patient had had since birth a pigmented mole about 1 cm. in diameter in the left cervical region. During 1926 a brownish area developed around the base of the mole about 2 cm. in diameter. In May, 1927, the lesion was removed by electrocoagulation. The microscopic report was non-malignant nevus pigmentosus.

Within three months, the patient noticed nodules in the left submaxillary and upper cervical regions and in a few weeks numerous small metastases appeared over the thorax anteriorly and in the right axilla.

On April 26 and 27, 1929, one series of deep roentgen therapy was given over the manifest metastases. The latest information is that this patient is deteriorating rapidly.

Case viii. A. W., female, white, aged forty.

This patient had two pigmented moles which had persisted unchanged for many years. One was in the right supraclavicular region and the other in the left flank.

The family physician delivered this woman early during 1927 and noticing the mole on the flank urged its removal, advancing the argu-

Fig. 5. Aggregated nodules of melanosarcoma developing in place of a pigmented mole destroyed by electrocautery (Case viii).

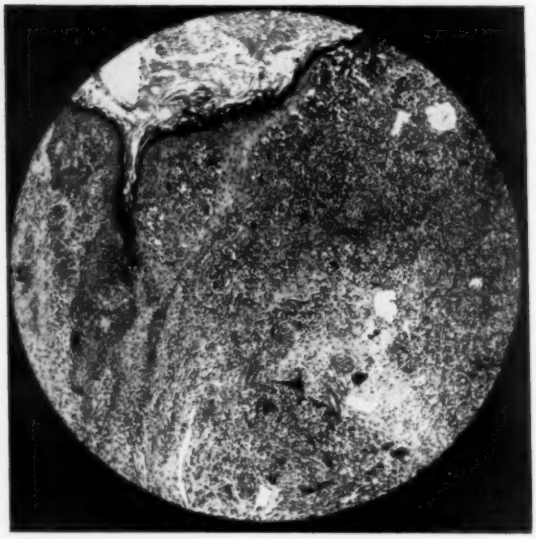

Fig. 6. Microscopic section of pigmented mole removed by surgical diathermy in Case ix. Low power. Melanotic lymphangioma hypertrophicum, non-malignant.

ment that it might develop into cancer. His advice prevailed and the mole was destroyed by the electrocautery. Within a few days there was local healing.

Within two months, however, several new moles appeared in the region of the original growth, these increasing rapidly in size, reaching 3 or 4 cm. in diameter.

On October 4, 1927, she consulted a surgeon who removed all the moles making a very wide elliptic excision. The microscopic report was melanosarcoma. Again within a few months following the operation, the moles recurred and the inguinal lymph nodes were invaded.

In March, 1928, she received the usual deep roentgen treatments in conjunction with colloidal lead given intravenously. These were continued at proper intervals until January 25, 1929. Later distant lymph nodes, skin, lungs and liver were invaded and the patient died on May 14, 1929.

Case ix. S. S., white male, aged fifty-six.

Late in 1926 this patient noticed for the first time a small growth of the scalp in the right parietal region. By November, 1927, the mass had grown to a diameter of about 2 cm. At this time silver nitrate as a caustic was applied. On January 13, 1928, the growth was removed by surgical diathermy, the microscopic report being non-malignant melanotic lymphangioma hypertrophicum (Fig. 6). Healing was delayed, so a second removal was done on February 10, 1928, by knife, with wide excision. The same pathologic report was returned on this tissue.

Within the month an enlarged lymph node was discovered in the right cervical region and soon another in the left axilla. At this time the possibility of a malignancy was considered and after studying numerous sections of the tissue removed at the second operation the pathologist discovered a few areas which could be interpreted as suspicious of malignancy (Fig. 7).

From February, 1928, to April, 1928, two series of deep roentgen treatments were given to the regions which are known to be the most common seats of metastases, the site of the primary lesion not being exposed. In August, 1928, a recurrence developed in the scar of the primary lesion, consisting of several nodules of dark blue color (Fig. 8). This area was treated on September 10, 1928, by hypermassive radiation and local healing resulted within two months (Fig. 9). In the meantime, skin, lungs and liver were being invaded and the patient died on March 21, 1929.

While the deleterious effect of the traumatization by the various therapeutic agents employed is clearly manifested in all the foregoing instances (Cases vi, vii, viii and ix), Case ix is especially convincing.

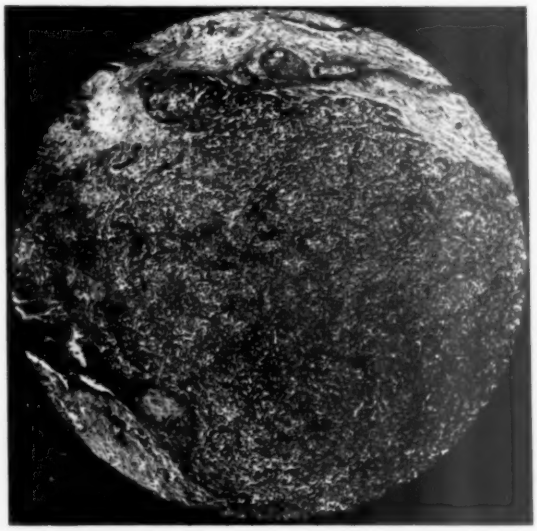

Fig. 7. Microscopic section of the recurrence in Case ix. Low power. After painstaking examinations, a few areas suspicious of malignant degeneration (melanosarcoma) were found.

An exhaustive microscopic study of the original mole failed to reveal any sign of malignancy, the report classifying the tumor as a "simple melanotic lymphangioma hypertrophicum" (Fig. 6). Likewise the pathological report on the tissue removed at the operation for the recurrence made no mention of malignancy, although by this time there was clinical evidence that a benign tumor was not being dealt with for nodules were observed in the cervical and axillary regions. A re-study of the tissue, using numerous serial sections, resulted in the finding of a few areas of cellular overgrowth with increased vascularity (Fig. 7), and this, with the clinical findings, justified a diagnosis of possible malignancy.

It is true that an apparently innocent histological picture of certain moles which have given rise to secondary tumors may be occasionally encountered and, according to Ewing[10] this forms "one of the most mysterious features of the disease." It remains, nevertheless, a fact that in our case the secondary tumors appeared shortly following the operative intervention, leading to rapid exitus. They must, therefore, be considered—as in the rest of the cases—the sequlae of the useless therapeutic procedures enumerated above.

Fig. 8. Small nodules of melanosarcoma developing in place of a pigmented mole removed by surgical diathermy in Case IX.

Fig. 9. Same as Figure 8, following hypermassive radiation with soft unfiltered roentgen rays. Local healing.

THE INFLUENCE OF EXCISION BY KNIFE

This question arises: Is the surgical excision by knife a better or safer procedure?

It is conceded that the majority of the investigators at this time favor the excision of the pigmented moles and melanomas with a wide margin and without injury to the pigmented area. Thus Christopher[6] says: "Excision is probably the safest method of removing moles. The moles and at least $\frac{1}{8}$ inch of the surrounding skin should be removed in one block, without cutting it or traumatizing it in any way. If local anesthesia be used, the injection should be well away from the lesion."

Likewise Francis Carter Wood[25] states: "Surgery is the only treatment for mela-

notic tumors, but the excision must be early and wide and must include the original nodes." Bloodgood,[3] not so sure of the value of surgical removal, advises the use of the knife only for benign moles, while for the malignant pigmented tumors he advises the cautery. He writes: "Benign pigmented moles, as a rule, can be removed with the knife. The pigmented area should be given a margin of at least ½ inch, and the wound can be closed. When I think the mole has become malignant, I always use the cautery instead of the knife." An early surgical removal of moles is advised also by Rose and Carless,[20] Stelwagon,[22] Boyd,[4] Gleave,[11] and others. Handley[12] in his Hunterian lecture on the melanomas recommends "The simultaneous removal not only of neighboring glands, but also the intervening lymphatics which are also implicated."

Broders and MacCarty,[5] and Coley and Houget[7] write: "The chief hope of reducing the mortality of this extremely fatal type of neoplasm must rest with prophylactic treatment, that is, the surgical removal of all pigmented moles as soon as observed, and particularly in all cases in which the anatomical locality renders them liable to irritation or to external injury. If this rule is rigidly followed, we believe the number of cases will be markedly diminished."

In analyzing available statistics on the end-results of the surgical treatment by knife as recommended above, one must sharply differentiate between the quiescent pigmented moles and the malignant melanomas. No satisfactory statistical studies of the first can be found. The impression given by most authors is that the method gives results approaching 100 per cent and that technically it is entirely harmless. In the second group, the few published reports are most discouraging. For instance, Broders and MacCarty[5] in 38 cases of "melanoepithelioma" operated on between 1904 and 1915 at the Mayo Clinic found only one case which passed the five year period (the patient dying eight years after the operation), and even this was a melanosarcoma of the eye—a type which is known to be less malignant than melanomas arising in the skin. The average duration of life after the last operation in the other 37 cases was eleven months and three days. Coley and Houget[7] in 81 personal and 14 cases collected from the literature found (by omitting 4 melanosarcomas of the eye) 6 cases which passed the five year period, 4 of them being irritated pigmented moles (without microscopic diagnosis) and only 2 definite melanosarcomas; and in these cases, most died within the first year following the operation.

Of 200 cases of "malignant moles" operated upon by Bloodgood[3] during a period of thirty years, there was a five year cure in only one instance. According to McEuen[15] this patient had some postoperative roentgen therapy and in his opinion "the X-ray therapy really produced this one cure beyond the five year period."

Gleave[11] in reviewing the operative results in 40 cases of malignant melanomas—22 arising in the skin and 18 in the eye—found that only 2 of the cutaneous cases survived the five year period. The average life duration in these cases was relatively high—two years and ten months.

Poor results were obtained also by Dawson[8] who says, "The generalization is said to average three years from the time of malignancy in the primary growth, but in my series it took place earlier in most of the cases."

Thus, with a practically 100 per cent mortality in the malignant melanomas, it would seem that the surgical treatment of pigmentiferous formations of the skin should be limited to the removal of the benign or quiescent moles. Since the great majority of the melanomas have their origin in pigmented moles, it would seem logical to practice excision as advised by Broders and MacCarty,[5] and Coley and Houget,[7] especially if the moles have been injured or are on exposed portions of the body.

A careful study of the cases of this group referred to our department for roentgen therapy, however, convinces us that such

a procedure carries with it the utmost danger. Not only is the excision of a pigmented mole, especially when irritated or traumatized, sometimes followed by a local recurrence, but not infrequently there is a widespread dissemination of melanotic tumors resulting in early death. The following cases prove this contention:

Case x. C. B. McP., white male, aged forty-three.

In 1920 this patient first noticed a pigmented mole on the inside of the right foot. Incident to repeated injury, this became infected. During 1923, the lesion slightly enlarged. At this time, roentgen treatment was given locally, with the advice from the roentgenologist that surgical removal was not to be considered. Disregarding this, and refusing further irradiation, he submitted to surgical removal of the mole on October 26, 1923, no microscopic examination being done. Within one month following the operation, the right inguinal lymph nodes became enlarged and later distant metastases made their appearance. From February 12, 1924, to April 26, 1924, the patient received numerous deep roentgen treatments. Death occurred on May 6, 1924. Post mortem examination revealed involvement of lymph nodes, mediastinum and esophagus and other tissues. The microscopic diagnosis was melanosarcoma.

Case xi. S. G. S., female, white, aged forty-one.

In this case, a pigmented mole had been present in the supraclavicular region since birth. Late in 1922, the patient thought the lesion was enlarging and she submitted to surgical removal with wide excision. The microscopic report was non-malignant pigmented nevus.

Two months later, the right cervical lymph nodes became enlarged. These glands were resected and at this time the pathologist reported melanosarcoma.

In December, 1923, roentgen treatments were begun. At this time there was no recurrence of the primary lesion but the right submaxillary and upper cervical regions presented glandular enlargements. This treatment period extended from December 27, 1923, to June 14, 1924, during which time the tumors extended to skin, lungs and liver. The patient died in the fall of 1924.

Case xii. R. K., white male, aged sixty-one. This patient gave a history of a pigmented mole being present on the anterior chest wall for several years. In March, 1924, this mole was surgically removed, no tissue being sent for microscopic study. Nine months later, or in December, 1924, the patient developed severe back pains and in January, 1925, numerous skin nodules appeared. We saw him on March 13, 1925, he having been referred for roentgen treatment. A skin nodule was removed for microscopic examination and the report was "very malignant spindle-cell melanosarcoma." Since there was already widespread involvement of lymph nodes and skin and invasion of liver and lungs, no treatments were given, the patient dying in June, 1925.

Case xiii. R.V. white male, aged twenty-nine. In this case a mole had been present on the back since birth. Some time in 1922, this was removed by surgery and no microscopic study was made. In January, 1925, enlargement of the left inguinal lymph nodes was noticed. Four months later one of these glands was removed for microscopic study, and the pathological report was "very malignant alveolar celled melanosarcoma." At this time extensive deep roentgen therapy was undertaken, exposing all the manifest metastases. The disease was not controlled and the patient died on October 9, 1925.

Case xiv. G.D., white male, aged fifty-one. A pigmented mole about 1 cm. in diameter had been on this patient's face since birth. Several times this lesion had been cut in shaving.

In Feburary, 1928, the patient considered that the mole had increased in size, and in addition there was irritation which persisted for several weeks.

In June, 1928, the mole was removed with wide excision. A microscopic study of this tissue revealed the presence of a melanosarcoma.

Within one month following the operation, the right submaxillary lymph nodes became enlarged and a second operation, in August, 1928, was done for removal of these. Within a month, additional tumors appeared. In February, 1929, we were requested to undertake deep roentgen therapy, but owing to previous failures, we declined. At this time the patient is rapidly deteriorating.

Case xv. E.D., female, white, aged thirty-seven. In the fall of 1923, this patient developed a peculiar lesion of the left small toe. A tentative diagnosis of osteomyelitis was made. In

Fig. 10. Disseminated nodules of melanosarcoma involving two-thirds of lower leg and ankle following amputation of the left little toe for primary melanosarcoma.

December, 1923, the diseased toe was amputated. The microscopic report made on the specimen was melanosarcoma.

Within three weeks following the operation numerous skin nodules appeared on the lower left leg (Fig. 10), and one month later a left inguinal lymph node became enlarged. From February 24 to April 24, two series of extensive deep roentgen treatments were given. The disease was not controlled and death occurred in the fall of 1924.

Case xvi. E.F., female white, aged forty-six. In this patient, a pigmented mole about 3 cm. in diameter had been present on the mons veneris for several years. During 1928, the tumor appeared to be growing slowly and her physician removed it, making a 2-inch elliptic incision. The microscopic report was melanotic lymphangioma hypertrophicum, non-malignant (Fig. 11).

New moles appeared in the region of the original lesion within eight months. These enlarged slowly and during this period the patient suffered from severe backache.

On November 26, 1929, a second removal of the moles was done, this time with a very wide excision and with resection of the inguinal glands. The microscopic report this time was a "very malignant alveolar celled melanosarcoma" (Figs. 12, 13 and 14). In November, 1929, she was given one series of deep roentgen therapy. The patient died on June 30, 1930, from general body involvement with this tumor.

In studying the course of the disease in the foregoing 7 cases, one cannot avoid being impressed with the rapidity with which the development of melanotic tumors followed the operative removal of apparently harmless moles or lesions. In Cases xi and xvi, the pathological report on the excised tissue indicated a benign growth and in Cases x, xii and xiii, no microscopic examination was considered necessary so certain was the clinical diagnosis of non-malignancy. Only in Cases xiv and xv was a diagnosis of malignancy made. Yet in all cases, except Case xiii, metastases developed within a few weeks or months and the postoperative life of the patients averaged less than a year.

In Cases xv and xvi, local recurrence accompanied distant development. Obviously

Fig. 11. Microscopic section of Case xvi, low power. Melanotic lymphangioma hypertrophicum.

the surgical excision of pigmentiferous formations occasionally constitutes a rather dangerous procedure, whether the melanotic area has already undergone a malignant degeneration or is still in a state of quiescence or inertia.

Holfelder[13] made a comprehensive review of the literature and a detailed study of his own cases with particular attention to the behavior of melanotic tumors after operation, and he expresses the following opinion: "It is commonly known that not only the biopsy of a melanotic tumor, but also the wide excision of a melanosarcoma is usually followed by generalized sarcomata." And again, "One cannot sufficiently insist on the great danger of an operative intervention; it is better to omit all surgical procedure than to hasten the dreaded dissemination of metastases and thus shorten considerably the patient's life."

THE VALUE OF RADIATION THERAPY

Having in mind the limited value and even the positive danger of all other therapeutic procedures, we were most anxious to determine the efficacy of radiation therapy in pigmentiferous formations of the skin. Here again, we must not confuse the benign pigmented moles and the already malignant melanomas.

From the literature, one determines that pigmented moles, in spite of some satisfactory results by Pusey[18] with roentgen rays, and by Wickham and Degrais[24] and Simpson[21] with radium, were soon considered resistant to radiation and therefore they were eliminated from the list of radiore-

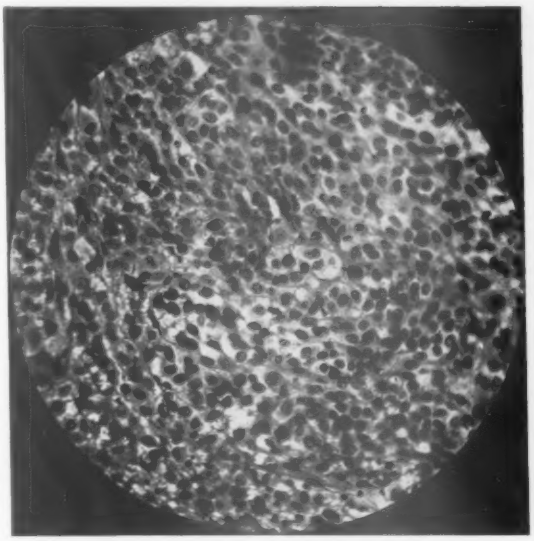

Fig. 13. Same as Figure 12, showing very malignant character of cells. High power.

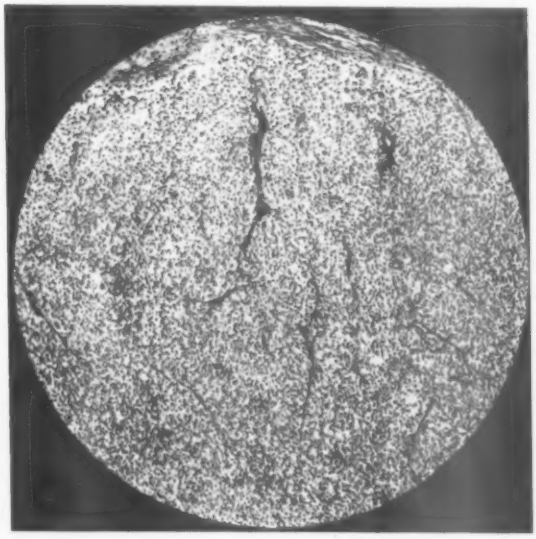

Fig. 12. Microscopic section of Case XVI, one and a half years later, showing malignant transformation: alveolar cell melanosarcoma. Low power.

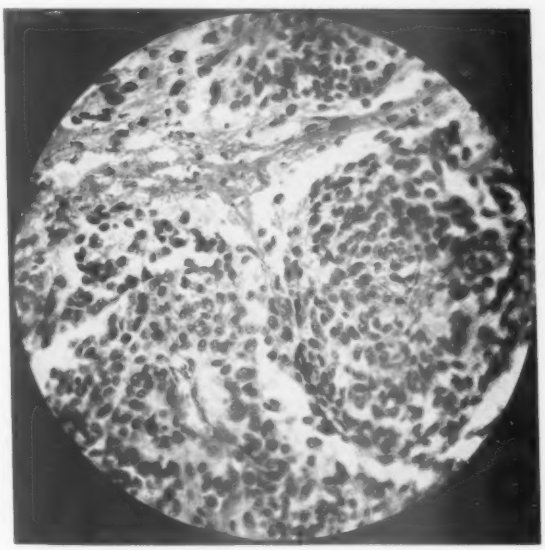

Fig. 14. Same as Figure 12, showing alveolar arrangement of cells. High power.

sponsive lesions. Thus McKee[16] makes this statement in the latest edition of his textbook: "The author is of the opinion that X-rays and radium are not indicated in the treatment of nevus pigmentosus," while Coley and Hoguet[7] go so far as to state that "the use of radium and X-rays in a pigmented mole or an operable melanoma is a most unwise procedure and attended with great risks."

As regards the second group, the malignant melanomas, the published opinions are at variance. Wood[25], agreeing with Coley and Hoguet considers radiation therapy directly harmful. Thus he writes: "The melanomata are but little affected by the most intensive radiation. Wide distribution often follows its application and the same is true of caustics, fulguration or freezing as so frequently practiced by the dermatologists."

Arzt and Fuhs[1], Werner,[23] and others, admit radiation therapy only in conjunction with surgery, as a postoperative measure. Thus Arzt and Fuhs write: "Every operable primary sarcoma of the skin must first be operated upon and only then submitted to radiation," while Werner makes the following statement: "It seems that radiation therapy, because of its slower effect, occupies a position which is inferior to that of the radical 'ignioperation,' the method of choice being a combination of surgery and radiation."

More recently an increasing number advocate radiation therapy, preferring it to any other method. Individual cures were obtained by Owen[17] in one case, Jeanneney and Mathey-Cornat[14] in 3 cases, Ratera and Ratera[19] in one case, Bérard[2] in 3 cases, McEuen[15] in 2 cases, Holfelder[13] in 2 cases, and others. McEuen and Holfelder insist that surgery in the treatment of malignant melanomas must be entirely discontinued, roentgen therapy being the sole method indicated.

In our service at Harper Hospital, we have used roentgen therapy for melanomas since 1922, and for pigmented moles since 1925, and at this date we have recorded 30 melanomas (melanosarcomas) and 21 pigmented moles. Since no microscopic examinations were made in this latter group, it is probable—as will be gathered from the description of a few selected cases—that some of them were true melanosarcomas. It should be mentioned here that most of the moles were either of the black adult type or of the irritated type, no attempt having been made to treat congenital vascular pigmented nevi or the hairy (pilosus) moles. (Two of this latter type were treated experimentally by hypermassive doses with temporary epilation as the only result.)

The vascular pigmented nevi are generally treated with radium or by plastic surgery.

For practical purposes in considering roentgen therapy, we divide the lesions included in the scope of this paper into three arbitrary groups:

1. Small primary pigmented tumors (not exceeding 5 cm. in diameter and 2 cm. in elevation) without extension.

2. Large primary pigmented tumors with or without lymph node extension, and the small tumors of Group 1 with lymph node metastases.

3. Pigmented tumors with extensive lymphatic, cutaneous and visceral metastases.

The lesions of Group 1 include the benign pigmented moles and the early malignant melanomas (a differential diagnosis without a microscopic examination is usually impossible), while the lesions in Groups 2 and 3 include only positively malignant melanomas (melanosarcomas).

1. *Small Primary Pigmented Tumors (Pigmented Moles and Early Melanomas).* In this group we use hypermassive radiation with soft, unfiltered roentgen rays. In a previous article[9] is given the principle and mode of application of this type of treatment. We might restate here that a "hypermassive" dose represents an amount of roentgen rays which produces a cytocaustic action of the tissues exposed and is equal to several erythema doses. On account of the very superficial character of the rays employed, the destruction is con-

fined to the upper layers of the integument, a complete healing resulting in a few weeks.

Technique. The lesion to be treated—and its size must conform to the limits above stated—and also 1 or 2 cm. of normal skin surrounding, are included in the field of irradiation, the remaining skin being heavily protected by lead. The dose corresponds to 100 to 125 ma-min. with the following factors: 62 kv. eff. (6 inch spark gap), no filter, 28 cm. skin target distance, 5 ma., 20–25 minutes, the entire dose being given in one application. As a result of this exposure, an intensive redness of the skin develops after a week, this continuing for two or three weeks. In certain cases, there is bleb formation, indicating a second degree erythema. By the end of the third week, there is scab formation, this being shed spontaneously in the seventh or eighth week, leaving a smooth scar. In rare cases only is it necessary to repeat the treatment. The second treatment should be delayed, for at times results from the first exposure are postponed to the fourth or fifth month.

If it is suspected that the pigmented tumor is becoming malignant, it is advisable to extend the radiation to the regional lymph nodes, using deep therapy for this purpose (according to the method for Group 2).

As already stated, 21 cases of this group were treated, all being classified, because of lack of microscopic report, as "pigmented moles." The immediate results were entirely satisfactory and so far there have been no recurrences and no cases of dissemination over a period of from two to five years. We include several striking cases, briefly stated.

CASE XVII. W.P.K., white male, aged sixty-two. A black pigmented mole about 1 cm. in diameter on the left temple had remained unchanged for some ten years. The patient noticed growth in extent and elevation during December, 1924. In January, 1925, his physician diagnosed the lesion as a melanosarcoma and urged immediate removal by excision. A medical friend vetoed this suggestion and referred him for roentgen therapy. When we saw him on January 26, 1925, a wart-like excrescence 1 cm. in diameter was present on the left temple. There was black discoloration and the appearance gave the impression of an irritated mole undergoing active growth.

A hypermassive dose of roentgen rays was given on January 26, 1925, the lesion and 1 cm. of normal skin being included in the field.

Healing followed in two months and there has been no recurrence after five years.

CASE XVIII. D.D., female, white, aged six. In this patient a pigmented mole had been present in the left axilla for four years. During 1925 one of the moles showed rapid growth and she was referred to Harper Hospital for roentgen therapy. Examination made on July 30, 1925, revealed a large papillary mole about 3 cm. in diameter and 1 cm. in elevation, apparently actively growing and showing intensive dark discoloration. There were three small pigmented nevi about 1 cm. in diameter near the large mole (Fig. 15).

On July 30, 1925, the large mole was treated by using a hypermassive dose and during the following months the smaller lesions were treated

FIG. 15. Pigmented mole of left axilla (Case XVIII).

Fig. 16. Same as Figure 15, following hypermassive radiation with soft unfiltered roentgen rays. Local healing.

in the same way. All moles disappeared, the only residue being a limited pigmentation within the remaining scar (Fig. 16). We have had no report on this case since December 19, 1925, so the present condition is unknown.

Case xix. S.B.R., white male, aged fifty-two. Here a pigmented mole on the anterior surface of the forearm, a few inches above the wrist, had persisted for fifteen years. Some fourteen years previously the mole was excised but it recurred promptly and remained unchanged until early in 1925, when it began to enlarge and became considerably darker in color. When seen on June 4, 1925, a small tumor about 3 cm. in diameter and of dark purplish color presented on the anterior aspect of the left forearm just above the wrist (Fig. 17). No lymph node enlargement was found. On this date, a hypermassive dose of roentgen rays was given in the usual manner to the lesion and surrounding zone of normal tissue, and the lymphatic drainage areas were treated with deep roentgen therapy. The lesion healed and the patient was well in July, 1928, the date of our last record.

Case xx. M.B., white male, aged fifty-six. This patient had a pigmented mole about 2 cm. in diameter on the left shoulder, which had been there since birth. A second smaller mole was present, lower and near the spine. In July, 1927, the upper mole increased in size and in October became ulcerated and infected. His physician treated him conservatively without result.

He was referred for roentgen therapy on December 1, 1927, at which time examination revealed an ulcerated pigmented mole some 3 cm. in diameter, on the left shoulder. There was induration of the edges with crater-like elevation (Fig. 18). There was a profuse discharge and bleeding occurred easily. No lymph node enlargement was detected. A hypermassive dose of roentgen rays was given at this time, and the regional lymph nodes exposed to deep radiation also.

The lesion healed within two months (Fig.

Fig. 17. Pigmented tumor of anterior aspect of left forearm (Case xix). Hypermassive radiation produced disappearance of tumor.

Fig. 18. Ulcerated pigmented mole of left shoulder (Case XX).

Fig. 19. Same as Figure 18, three years after application of hypermassive radiation with soft unfiltered roentgen rays.

Fig. 20. Pigmented mole of back (Case XXI).

Fig. 21. Same as Figure 20 three years after application of hypermassive radiation.

Fig. 22. Pigmented vascular nevus of lower eyelid (Case xxii).

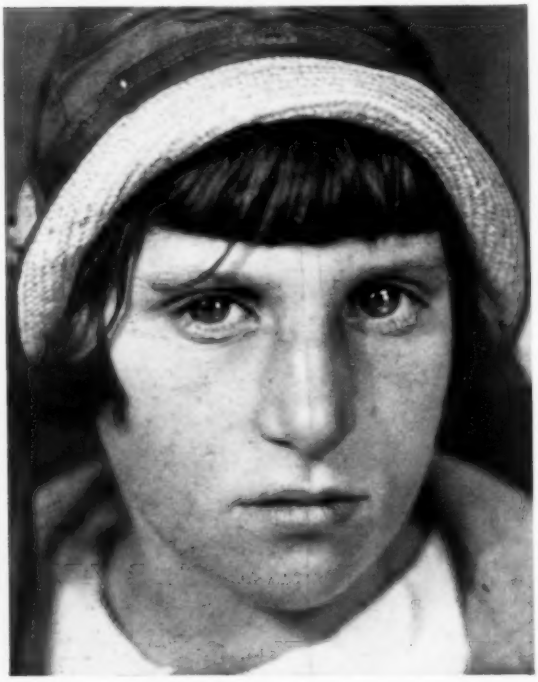

Fig. 23. Same as Figure 22, two and a half years following massive radiation.

19) and has not recurred, nor have secondaries developed to this time, three years later.

Case xxi. R.E., female, white, aged thirty. In this case a pigmented mole had been on the back since birth. This has been enlarging slowly since 1920 without signs of irritation. No attention was given to the lesion until May 16, 1927, when she presented herself for treatment of the mole.

At examination on May 16, 1927, there was noted a pigmented nevus of the back at the level of the seventh thoracic segment, oval in outline, 4.25×7 cm. in area and 0.5 cm. in elevation. The lesion appeared inactive (Fig.

Fig. 24. Adulted pigmented mole of left temple (Case xxiii).

20). At this time, a hypermassive dose of roentgen rays was given over the lesion and 1 cm. of surrounding normal skin. On account of the extensive character of the mole, both superficial and deep rays were used.

A marked reaction followed this treatment with the formation of a third degree ulcer. This persisted for nearly a year, healing not occurring until the base of the ulcer was subjected to electrocoagulation (Fig. 21). At this time, some three years later, there is no recurrence and no distant development.

Case xxii. M.D., white girl, aged ten. In December, 1927, the patient noticed for the first time a small mole of the mid-portion of the right lower eyelid near the hair line. This enlarged rapidly and took on latterly a purplish black discoloration.

Examination on March 7, 1928, revealed a tumor 1×0.5 cm. at the base, and of 1 cm. elevation, purplish in color and with areas of definite pigmentation (Fig. 22). The lesion was classified as a pigmented vascular nevus and treated by massive unfiltered radium (unfiltered plaque). One month later a filtered radium plaque was applied.

Fig. 25. Same as Figure 24, two and a half years after hypermassive radiation with soft unfiltered roentgen rays.

The lesion healed (Fig. 23) and has so continued for two and a half years.

Case xxiii. G.G., female, white, aged fifty-eight. This patient received treatment for breast carcinoma thirteen years before consulting us in connection with the appearance of two pigmented moles, one on the left temple and the other on the right check. These were first noticed in January, 1928, and in the following three months they showed considerable growth, especially the one on the temple.

Fig. 26. Adult pigmented mole of right cheek (Case xxiii).

Fig. 27. Same as Figure 26, two and a half years after hypermassive radiation with soft unfiltered roentgen rays.

Fig. 28. Adult pigmented mole of right lower eyelid (Case xxiv).

Fig. 29. Same as Figure 28, two and a half years after hypermassive radiation with soft unfiltered roentgen rays.

Fig. 30. Pigmented tumor of right temple (Case xxv).

Fig. 31. Same as Figure 30, two years after hypermassive radiation.

On April 13, 1928, the mole of the left temple was 1.5 cm. in diameter (Fig. 24) and the other about one-half the size (Fig. 26). Neither showed much elevation and they were apparently quiescent. Both lesions responded to hypermassive roentgen radiation with soft and unfiltered rays, healing occurring within two months (Fig. 25 and 27). After two and a half years, there is no recurrence. The breast carcinoma continued controlled.

Case xxiv. I.D., female, white, aged forty-three. This patient reported the appearance, in 1918, of a small pigmented mole on the right lower eyelid. In 1923 this was removed surgically. In 1927 there was a recurrence with gradual growth. In January, 1928, when we were consulted, a small mole 0.5 cm. in diameter and 0.25 cm. elevation presented on the right lower lid (Fig. 28). This healed in response to a hypermassive dose of roentgen rays (Fig. 29) and there is no recurrence after two and a half years.

Case xxv. E.S., female, white, aged sixty-nine. In June, 1927, this patient noticed for the first time a small pigmented mole of the right temple near the hair line. Growth was rapid, with considerable elevation. This mole was repeatedly injured during hair combing, leading to ulceration and bleeding. Since April, pigmentation had occurred. On June 27, 1928, an examination revealed a deep black tumor of the right temple 2.5 cm. in diameter and 1 cm. elevation (Fig. 30). No lymph gland enlargement was found. On this date, the lesion was treated, using hypermassive radiation with soft unfiltered roentgen rays.

The lesion healed within two months (Fig. 31) and now, two years later, there is no recurrence and no signs of extension.

2. *Large Primary Pigmented Tumors (Melanosarcomas) with or without Metastases.*

If a tumor exceeds 5 cm. in diameter and 2 cm. in elevation, the hypermassive radiation with soft unfiltered rays is not effective because of the low penetration of these rays. The lower strata of cells with this exposure would receive insufficient radiation and consequently, after a period of growth restraint, would begin to multiply, leading to recurrence. On the other hand, the administration of rays of greater penetration would produce an injury too severe for the normal tissues. This difficulty can be met in one of two ways. First, a massive roentgen dose with mixed wave lengths can be used, or, second, roentgen therapy and surgical therapy may be combined.

In the first instance, we give a basic dose of 100 per cent s.u.d. with deep roentgen rays (0.13 Å eff. wave length), and then attempt to make up a cytocaustic dose by the addition of soft unfiltered roentgen rays (the amount of this latter depending on the size and location of the tumor).

In the second method, a 100 per cent s.u.d. of deep roentgen rays is administered and after an interval of three or four weeks, excision of the tumor is done. It is wise to attempt the mixed radiation first and only in case of failure resort to the combined method. When the regional lymph nodes are involved it is advisable to resect those thoroughly and follow with extensive postoperative deep roentgen therapy.

We have but 5 cases in this group, 2 of which died from early spread of the disease. Three have remained well for eight, seven and one-half and four and one-half years respectively, and these reports are as follows:

Case xxvi. S.L., female, white, aged forty-nine. In 1918 this patient noticed a small mole on the little finger. This gradually enlarged and in 1920 the lesion was removed without microscopic study. In February, 1922, axillary lymph node enlargement was noticed. These were removed surgically on August 7, 1922, and examined microscopically, the pathological diagnosis being spindle cell melanosarcoma (Figs. 32 and 33). Two weeks following the operation, one series of deep roentgen treatments was given, exposing the left axilla, left cervical, infra- and supraclavicular regions and mediastinum. In March, 1923, this treatment was repeated. The patient continues well after an interval of eight years.

Case xxvii. R.O., white male, aged fifty-nine. Since 1917, a pigmented mole about 1.5 cm. in length had involved the left little finger. Up to January, 1923, there had been no appreciable growth, but following this, enlargement was rapid. This tumor was removed by

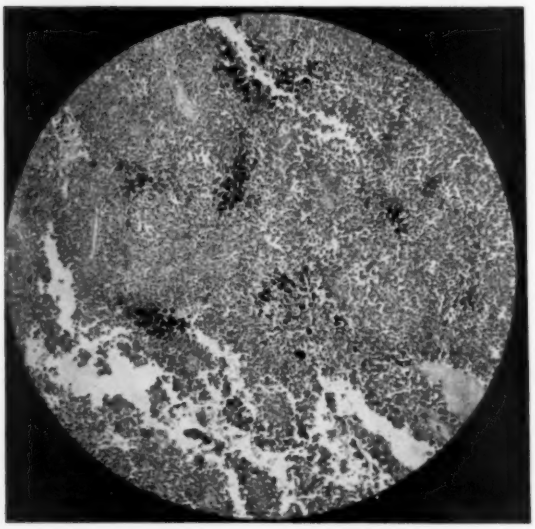

Fig. 32. Microscopic section in Case xxvi showing very malignant melanosarcoma with marked abundance of pigment. Low power.

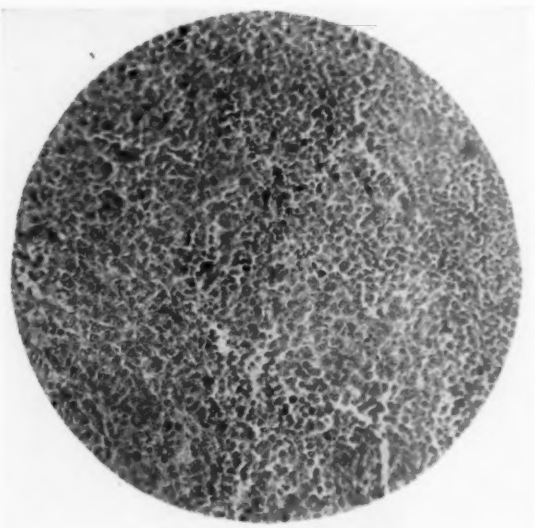

Fig. 33. Same as Figure 32. High power.

wide excision on March 4, 1923, and pathological report was melanosarcoma.

On March 20 and 21, 1923, this patient received deep roentgen treatments over the site of the primary lesion, as well as over the regional lymph nodes (epitrochlear, axillary, supra- and infraclavicular and cervical glands of the left side). No recurrence or distant metastases are evident after a period of seven and a half years.

Case xxviii. T.P., female, white, aged fifty. This patient had several congenital moles on various parts of the body. In the fall of 1925, one of these on the right breast increased in size. In October, 1925, her physician advised its removal, which was done surgically. No tissue diagnosis was made. Promptly following this operation, an enlarged lymph node was found in the axilla. This grew rapidly and by April 1, 1926, its diameter was 6 or 7 cm. On this date, a second operation was done which included thorough resection of all the axillary glands. The tissue diagnosis was "very malignant melanosarcoma." From April 1 to April 9, 1926, deep roentgen treatments were given exposing the right axilla, right supra- and infraclavicular regions, the mediastinum and upper abdomen. At the present time—an interval of four and a half years—there is no recurrence or evidence of distant growth.

3. *Pigmented Tumors (Melanosarcomas) with Extensive Lymphatic, Cutaneous and Visceral Metastases.*

Twenty-five of our melanosarcomas belonged to this group. All were practically hopeless, the usual methods of treatment having failed. In 6 the condition was so precarious that roentgen treatment could not even be attempted. Of the remaining 19, in 3 cases temporary improvement was brought about by deep roentgen treatment and life was prolonged for four or four and one-half years. The average life duration of the remaining 16 was a little more than a year.

The technique of irradiation in this group was that generally used for other types of malignancies. Our factors are 200 kv., 1 mm. Cu, 1 mm. Al, λ eff. $=0.13$ Å, 90–120 per cent s.u.d., 600–750 r (in air), the number of areas depending on the extent of the disease.

The 3 cases in which life was prolonged are as follows:

Case xxix. W.B., white male, aged forty-four. In January, 1922, this patient noticed that he was losing the nail of the right large toe due to a new growth beneath it. In March, 1922 this new growth ulcerated. There was no his-

tory of trauma. On June 20, 1922, examination revealed an ulcerated lesion of the right great toe about 1.5 cm. in diameter and enlargement of the inguinal lymph nodes, some of these having a diameter of 3 cm.

On June 21, 1922, the involved member was amputated proximal to the end of the first metatarsal. The microscopic report was that of advanced alveolar spindle celled melanosarcoma.

From June 24 to 29, 1922, deep roentgen treatments were given over the popliteal, inguinal and pelvic lymph nodes and over the mediastinum. A second series was to be given in seven weeks, but the patient did not return until February 5, 1925, at which time there was evidence of recurrence in the right groin. A second series of deep treatments was given from February 25 to March 3, 1925, with only temporary improvement. The disease continued to spread and death ensued in the fall of 1926, giving an interval of four and a half years.

Case xxx. M.B., female, white, aged thirty-eight. In this case a pigmented mole just above the right iliac crest had persisted since birth. No change in size was noticed until June, 1921, when growth suddenly started. Surgical removal was done a few months later, the microscopic report being "very malignant melanosarcoma."

In April, 1922, enlargement of the axillary nodes was noticed and in a few months similar changes occurred in the right cervical group.

In November, 1922, she was referred for deep roentgen therapy. At this time the melanosarcoma was well generalized with tumors in all the superficial lymph node groupings and with cutaneous nodules over the abdomen.

From November 23 to November 28, 1922, deep roentgen exposures were made over the entire lymphatic system, chest and abdomen with special attention to the manifest metastases. As a result of this treatment, all of the enlargements disappeared and the patient continued well until 1925, when extension to the bony structures developed. A second series of deep roentgen treatments brought about only temporary improvement, and patient expired on December 27, 1926, with an interval of four years.

Case xxxi. J.A.E., female, white, aged thirty-eight. Since birth a pigmented mole had persisted in the right epigastric region. In 1924, when growth appeared to be enlarging, a physician was consulted and he treated the lesion by ligation. The mole separated in a few weeks. Six months later, or in December, 1924, the patient noticed masses in the right axilla. These were removed in February, 1925, the tissue report being melanosarcoma.

In March, 1925, several new moles appeared near the site of the original lesion in the epigastric region. These were removed with a wide elliptic incision and the pathological report again was melanotic alveolar sarcoma.

From April 26, 1925, to April 30, 1925, this patient received a very extensive course of deep roentgen therapy over the entire lymphatic system, the site of the primary lesion and the lungs and liver. No recurrence was evident after a four year interval, but the patient died from an unknown cause in a neighboring city.

CONCLUSIONS

The pigmentiferous formations of the skin may be divided into two main groups: the pigmented moles (nevus pigmentosus) and the melanomas (melanosarcomas). The former, as a rule, are harmless, while the latter represent the most malignant of neoplasms.

The relation of the two processes is of great clinical importance, inasmuch as pigmented moles, under the influence of trauma or chronic irritation, may transform into malignant melanomas.

Therapeutic procedures which have a traumatizing effect, as, for example, electrogalvanization, fulguration, application of CO_2 snow, cautery, electrocoagulation (diathermy), etc., may change a pigmented mole into a melanoma or may disseminate an already existing melanoma; in consequence they must be rejected.

Operative procedures, with wide margins, did not materially influence the course of the disease in melanosarcomas, the five year mortality remaining practically 100 per cent. The prophylactic removal of all pigmented moles, and especially of those traumatized or exposed to irritation, as advised by some authors, is a dangerous procedure, not infrequently leading to malignant degeneration with rapidly fatal outcome.

Roentgen therapy is the treatment of choice. Congenital pigmented moles, if in a state of quiescence, must be left alone. Adult, and all traumatized and irritated moles, respond well to hypermassive radiation with soft unfiltered roentgen rays. Their removal by this method, judging from 21 personal cases, is entirely harmless. Malignant melanomas (melanosarcomas) are best treated by radiation therapy or, in carefully selected cases, by a combination of surgery and radiation therapy. Cures are observed not infrequently and prolongation of life may be obtained even in apparently hopeless cases. Of 30 cases of melanosarcoma in our series, 6 were in too precarious condition to be treated, 3 were cured, 3 lived four to four and a half years, and 18 died earlier, the average life duration after treatment being a little more than a year. It is probable that several cases of early melanoma were included in the group of the 21 "pigmented moles" primarily treated by radiation. The results in all these instances were very satisfactory.*

* We are greatly indebted to Dr. P. F. Morse, chief pathologist at Harper Hospital, for his invaluable assistance in working up the pathological material for this article.

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DISCUSSION

Dr. G. E. Pfahler, Philadelphia. I am a great admirer of Dr. Evans and his work, and, naturally, many of the things that he has said to you I can agree with, but in a number of very essential things I must very definitely differ in this instance. I did not have the privilege of reading his paper and, therefore, my remarks must be based upon what I have heard during the presentation.

In the first place, if he will insert in front of the words "electrocoagulation excision" the word "complete" it will change the whole atmosphere of this subject. I have treated by electrocoagulation certainly thousands of cases and thousands of pigmented moles, melanosarcomas, some of these being definitely and microscopically malignant. I think there is very great danger in tampering with any mole or melanosarcoma, whether it be benign or malignant. Therefore, any excision or incision or examination to determine whether or not it is malignant is absolutely bad technique. I am very glad Dr. Evans showed the two cases on the screen because we know now to what he refers. The one with the recurrence locally in the hair was certainly most incompletely removed, for you could see the growth of hair in what was spoken of as the scar. You cannot remove any mole or melanosarcoma completely without leaving a very complete scar and anyone who attempts to do it otherwise is only meddlesome. I have never seen a local recurrence in any of the moles or melanosarcomas that I have removed. I am sure they will run into the thousands, though I did not have time to review and check all the cases. I have only seen one case in all of these which developed metastasis afterwards and that was definitely and microscopically malignant at the time it was removed. There was no local recurrence, but the patient did develop metastasis in the lungs which I believe was present at the time I started my treatment, though, unfortunately, I did not make a film to show the absence or presence of any such lesions at the time.

With a record of that kind, certainly we cannot condemn electrocoagulation as a method of treatment, but improper electrocoagulation or incomplete electrocoagulation is very much like treatment with caustics, like incomplete treatment with caustics or incomplete treatment with the thermocautery, or incomplete excision. I am convinced that excision by the electrothermic method is better than excision by the knife.

Dr. Vastine very hastily got together 20 cases of malignant melanoma or malignant sarcoma, as they happen to be indexed, before I came away. Of these, 12 were extensive metastases and local recurrences following excision which in itself is a very poor record of excision, and all of these died in spite of anything that I could do. I have only succeeded in causing the disappearance of the metastatic lymph nodes in two cases in which they were present, and in only one of these did we get the patient permanently well. In the other case in which the local lesions disappeared, the patient developed metastasis elsewhere and we lost out.

I, in contradistinction to Dr. Evans, have not treated with the roentgen ray any pigmented moles or melanomas for twenty years. If you treat by irradiation, you must treat as Dr. Evans has done, sufficient to produce a definite local necrosis, in other words, a sloughing out of the process by much the same process as if you destroy it by some other means, as he uses a soft destructive dose of radiation.

I am just a little bit more certain of my destruction if I do it before my own eyes. When I believe the lesion is malignant or when there is any question of malignancy in my mind, I surround the lesion at present (I haven't always done this) by a deep electrocoagulation line so that I can completely and evenly pass the needle under the lesion, so that I can lift out the lesion completely without any chance of dissemination during the process. I then send that for microscopical diagnosis. That is what I did with a case in which later I got metastasis and the only one of all of these cases that ever developed metastasis.

I would like to throw on the screen a few cases to illustrate the points that I am making.

(Slide) In this first picture I am dealing with a recurrent malignant melanoma. This pigmented mole is a recurrence following an excision by a surgeon. This patient had malignant or rather pigmented moles on both sides of her neck for many years. She said all her life. In this case I carried out the technique which I have just described. I surrounded this lesion by an area of destruction, then I excised the lesion

for microscopical examination, and it was found very definitely a malignant melanoma. I then destroyed the other two moles which had not been touched on this right side of the neck, with this result—smooth healthy scars. This was in 1923; that patient is well today. That is seven years.

(Slide) This is the other side of that very same patient's neck, with the same character of moles that she had previously on the opposite side. You will see the result there, which is also permanent.

(Slide) Here again we have a recurrent malignant melanoma. The middle picture shows the effect after my destruction. That is the wound that I left—a very definite and complete removal. The third picture shows the end-result after the patient has recovered. You see that was 1927. That will also illustrate to you that when I remove these lesions, and particularly if it is malignant or thought to be malignant or a recurrent malignant melanoma, I do not play with the thing, I do it thoroughly. When you are dealing with a recurrence like that, you must almost assume that you may have metastasis. Certainly you must look for it and in that case we immediately made films of the chest and, of course, palpated everywhere, but found no evidence of disease. The patient is well; fortunately, it was a local recurrence.

(Slide) We get so many patients that say, "Oh, I can't touch these moles. I have them all over my body." I am showing you here a case in which I removed, as you will see, quite a number, about 500, of these pigmented moles, did them all under local anesthesia, with the result that you see on the right. That is six years ago. I believe in contradistinction, again, to the author of the paper that all pigmented moles should be removed. That is the best advice. It isn't essential, probably not more than one in a thousand will become malignant. We have no statistics to know just how many of these will become malignant. If it were my body, I would rather not take that one chance out of a thousand, because if it does become malignant, your chances of death, or the patient's chances of death as a result are very great.

(Slide) There is an extensive lesion. That was a malignant lesion as shown microscopically. It had not been previously treated. I did surround this before taking my specimen. It had all the appearances of being malignant and it was found microscopically malignant. There was never any local recurrence, but you can also see there is a real scar. There are no hairs growing through that scar.

(Slide) There is the lesion in the lung which appeared later and from which the patient died. This illustrates my position, and I believe that we are justified in recommending complete removal of all pigmented moles, but no tampering with any of them by any means whatever.

Dr. R. H. Stevens, Detroit, Mich. I think we must always remember, when we are dealing with moles, whether pigmented or not, particularly if they are irritated, that there may already be a metastasis developing. One case I had a number of years ago with a pendulous mole on the cheek, not a pigmented mole, but it was extending down perhaps half and inch and was becoming somewhat irritated. I wanted the patient to have this removed by electrocoagulation. She was a public speaker and didn't want the disfigurement just then. She postponed it for about two months. The next time I saw her, was in the hospital, when she was referred by the G. U. Department for examination of the kidneys. In getting a roentgenogram of the kidneys, we found tumors in the chest. She died in a very few weeks of metastatic melanoma. If I had taken that mole off with electrocoagulation or given it a heavy dose of roentgen rays or something of that kind, probably I would have had the credit of killing that patient with the treatment that I gave.

I have been taking off moles and warts by galvanic electrolysis for many years, way back twenty-seven years ago. Later on, I did it by electrocoagulation and I do practically all of them now with electrocoagulation. I have never yet seen one of those cases that I have treated by either method that has had any metastatic recurrence. This one I speak of is the only one that I have had that came to me primarily that had a recurrence, and I didn't treat that.

I have seen metastasis occur in a considerable number of patients following removal of moles, unpigmented, as well as pigmented, by the cold knife. I believe that method is a very dangerous procedure.

When we talk about electrocoagulation or about roentgen radiation, I think we should specify the details of the treatment that they receive. I can easily understand how a person might have a mole injured and have considerable harm done by electrocoagulation if the proper method is not pursued, as Dr. Pfahler says,

if a thorough job is not done. But I think if the work is thoroughly done that electrocoagulation is certainly by far the best method, and I don't believe that there is any danger from that method of treatment.

Dr. Evans (closing). The remarks of the discussants support my expressed plea for a more accurate classification of these lesions. Undoubtedly the results obtained by them are as they have stated, but they have dealt with the benign tumors and not with those already undergoing malignant degeneration.

Having in mind what Dr. Skinner said yesterday in his discussion of Dr. Erskine's paper, it may be that Dr. Pfahler and Dr. Stevens obtain their good results because they employ a proper technique and carry it out correctly. Yet the cases which I have reported are authentic and are from our records, and if we can draw conclusions from these, the use of electrocoagulation and similar forms of treatment is attended with grave dangers. Dr. Pfahler admits at least one case in his series developed recurrence or metastatic spread following such treatment and with others less skillful, such complications will be more frequent. We urge the use of the technique given in our paper, believing it to be the safest.

IDIOPATHIC HEMORRHAGIC SARCOMA*

REPORT OF A CASE TREATED BY ROENTGEN RADIATION

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INDIANAPOLIS, INDIANA

THIS interesting disease was first described by Kaposi[8] in 1872. He reported 5 cases and later added others. Since that time numerous authors have added to the literature on this subject, most of it being found however, in the journals of dermatology. Our concern is chiefly with its treatment by means of the roentgen ray.

Stelwagon and Gaskill[19] state that, with rare exceptions, the malady begins on the extremities, usually simultaneously, and this agrees with other reports. So constant is this finding that some authors deny that lesions first beginning elsewhere belong to this type of tumor.

Sequeira[18] reports that in 73 cases collected from the literature, all but 5 were in males. These 5 were regarded as doubtful cases since the lesions began on the trunk instead of the extremities. Most of the men were robust foreigners and from the lower classes. There have been few cases in native-born Americans.

Oulmann's[11] youngest case was thirty-three years of age. A few younger cases have been reported, Packard's[12] being only six months of age. This is the exception, however, as most of the cases are fifty or over.

The disease usually begins as a single small lesion. It spreads rapidly so that when first seen there may be numerous nodules over all extremities and perhaps over the body. They are purplish to dark blue, depending upon their location. The single nodule may be mistaken for angioma. Rosen's[14] case presented ulcerations and this is a likely complication.

Our case, as did many others, showed marked thickening of the skin, especially on the plantar surfaces of the feet. Many cases are hard to distinguish from scleroderma with nodular formations. All reports show varying degrees of edema in the lower extremities and late in the disease metastasis is likely to occur.

There is considerable controversy over the histology of this curious disease. Dillard and Weidman,[4] after an extended study, state that the lesions begin in the upper layers of the corium. The primary change is found in the capillaries, consisting in irregular hyperplasia accompanied by lymphangiectasia and hemorrhage. Secondary changes consist in accumulations of lymphocytes around the capillaries, together with nests of embryonal cells to which is added fibrosis. They believe it to be primarily an inflammatory lesion which secondarily becomes sarcomatous.

Ewing[5] says that it is an infectious granuloma of unknown origin which, in its later stages and under suitable conditions, may take on genuine neoplastic properties. The entire vascular system seems to be overtaken by degeneration with overgrowth of vaso-formative cells, leading in many instances to tumor formation.

Pautrier and Diss[13] state emphatically that Kaposi's disease is not a true sarcoma but a neurovascular dysgenesis. They found no tumor cells in their section. Campana,[3] Semenow,[17] and Saphier,[16] also make mention of it as a nerve lesion, and the latter points out the spread of the lesion along the nerve sheath to establish its connection with the nervous system. Semenow's belief in the nerve origin is based upon the presence of pigment in the cells of the spinal ganglia and upon the changes in the cells themselves.

Until recent years the prognosis in this disease has been regarded as bad, various authors giving the duration of life as from four to ten years. Brayton's[1] case was alive twenty-five years, and a few other exceptions are found. There have been a few

* From the Radiological Clinic of Drs. Cole, Beeler and Smith.

spontaneous cures. Medication has not been satisfactory.

Death results from visceral metastasis or, according to Ewing,[5] by extensions to the viscera. Dillard and Weidman[4] reviewed 9 cases and added one of their own in which visceral lesions were associated at autopsy. These occurred in all the organs of the abdomen and chest and in the lymph nodes. Hartzell[7] cites Bernhardt's case as showing that the bones of the extremities may be involved. It was found that the phalanges, with some of the metatarsal and tarsal bones, were almost completely destroyed. He does not say whether this was by metastasis or contiguity.

With the advent of roentgen therapy in these cases the prospect of cure became brighter although it has not been highly successful until recent years. Lustgarten's[9] case improved markedly, especially the pain, and the patient was able to walk. Halle[6] saw better results with roentgen therapy than from other procedures. Bulkley[2] presented a case before the New York Dermatological Society which had been treated with the coil machine and bare tube. No new lesions occurred in the treated areas. Williams[20] mentions the case treated by Bulkley in which marked improvement occurred but roentgen ulcers developed and treatment was discontinued. Two years later the ulcers had healed and the disease seemed arrested. Hartzell's patient showed marked improvement after a large number of treatments. Rosen's case was treated unsuccessfully by this method, probably because the dosage was too small.

MacKee[10] has a series of 9 cases, 7 treated by unfiltered roentgen rays and 2 with filtered beta rays of radium, all with excellent results. All were cured or kept under control.

Rosh,[15] in a more recent article, reports 2 successful results with high voltage roentgen therapy after other methods had failed. He employed 200 kv., 4 ma., 40 cm. distance, 0.5 mm. zinc and 1 mm. aluminum filtration; size of field as large as could be covered. Treatments were alternated over different fields at weekly intervals. After two months each patient was able to wear normal shoes and return to work.

CASE REPORT

C. G., aged seventy-two, was referred to our office by Drs. Oliver Ormsby of Chicago and E. P. Sloan of Bloomington, Ill., July 20, 1927. He was a large robust man but walked with the aid of crutches.

He complained of numerous pea-sized swellings over both feet and legs, also over the left forearm and palm of the left hand. He stated that a small "pimple" first appeared on the middle toe of the left foot about five years before. This later spread over both feet and legs. Three years later the tumors appeared on the hand and forearm.

The appearance of numerous reddish nodules over the regions described was typical of hemorrhagic sarcoma (Fig. 1). In addition there was

Fig. 1. Idiopathic hemorrhagic sarcoma before treatment. Note marked cornification.

a large amount of cornification, especially over the feet, and considerable edema. The lesions were not tender and there was no ulceration. There were no symptoms suggesting metastasis.

Roentgen therapy was given over all the involved parts, the treatments being continued for fifteen months, with gradual improvement. New lesions made their appearance above the knees but did not spread further. Factors used were 120 kv. (peak), 5 ma., 12 inch distance, 4 mm. aluminum filter. The average time of each treatment was ten minutes (approximately 66 per cent skin erythema dose). Two days were

taken when all areas were to be covered and during the first four months five series of treatments were given. So much roentgen radiation had been given that we felt it advisable to await results. Definite improvement was noticed at this time (Fig. 2).

On October 10, 1928, a few lesions had developed above the knee. These, with some on the hands not previously treated, were given three to four treatments with the above factors. Three months later when observed, all lesions had disappeared, also there had been a complete desquamation of all cornified areas. The skin was smooth and somewhat atrophic (Fig. 3). The edema was absent and the patient had been working for some time in complete comfort.

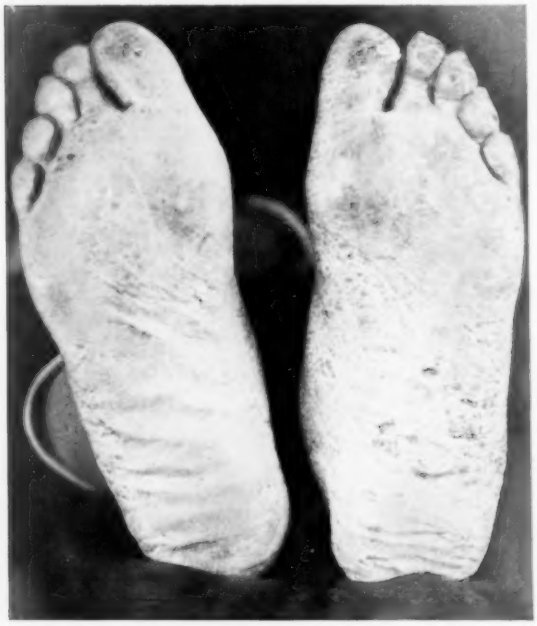

Fig. 2. Idiopathic hemorrhagic sarcoma, showing improvement after first treatments.

COMMENT

A case of Kaposi's tumor is reported where at least a temporary cure resulted from moderately heavy roentgen treatment. We believe that failure to obtain results in some of the earlier cases was due to too small a dosage. In a case of this nature, filters are essential. The treatment is a tedious, long-drawn-out process but the result justifies the effort if this case and others mentioned above can be taken as a criterion.

Fig. 3. Idiopathic hemorrhagic sarcoma seventeen months after first treatment.

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A CASE OF TUBERCULOUS DACRYOCYSTITIS TREATED WITH ROENTGEN RAYS

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THE ophthalmologists of Japan are regularly applying roentgen therapy for certain lesions of the eye and they are fully aware of its value. A few of the more recent publications are: "A case of rodent ulcer of the cornea" by Shimazu; "The radiation therapy of retinal glioma" by Kusama; "The changes of the tumor cells of the retinal glioma through X-ray irradiation" by Matsumoto; "A tumor of the sella turcica treated effectively with X-ray" by Nojiri; "A case of intraophthalmic sarcoma for which X-ray treatment gave good results in a short time" by Matsuda, and "A case of treatment for cancer of the lacrymal gland which followed an interesting course" by Matsuo. Lately Iizuka reported 12 experimental cases demonstrating the great value of the method. Generally, roentgen therapy is applied for the following eye conditions: palpebral diseases, trachoma, lesions of the lacrymal sac, and for certain conditions of the orbital and cranial cavities and of the intracerebral ventricles.

I have recently treated a case diagnosed as tuberculous dacryocystitis, and since the results obtained by roentgen therapy were so satisfactory, I now take the opportunity of adding this case to the literature.

CASE REPORT

Female, aged eleven, first examination Aug. 22, 1929.

Complaint. A redness and swelling in the region of the lacrymal sac.

Previous History. The patient had never been ill except for occasional colds and general debility. She had had a swelling in the region of the left lacrymal sac for one year, however without much distress. One week previous to her admission to the Out Patient Department, the swollen area became reddened.

Present Condition. Undernourished patient of a scrofulous constitution. There was some swelling of the cervical glands on both sides. In the region of the left lacrymal sac, there was a swelling the size of the end of a thumb, reddened and near suppuration. There was no pain and therefore the patient would not submit to operation. Wassermann negative; Pirquet positive. No involvement of eyeball proper.

The surgical diagnosis was tuberculous cervical lymphadenitis.

The ophthalmological diagnosis was tuberculous dacryocystitis.

Treatment. Roentgen therapy. Heliopan apparatus, Coolidge tube. First treatment, August 22, 1929, 125 kv., 4 mm. Al, 2 ma., 25 cm. skin target distance, field 22 mm. in diameter (size of lead glass cylinder), 6 minutes, 1/10 skin unit dose over the region of the left lacrymal sac. Second treatment, August 24, 1929, 130 kv. 0.5 mm. Zn and 1 mm. Al, 7 minutes, the other factors remaining unchanged. Third treatment, August 28, 1929, the technique being identical with that of the second. Fourth treatment, August 31, 1929, the technique being identical with that of the first. Fifth treatment, September 6, 1929, the technique being identical with that of the second. Sixth treatment, September 16, 1929, the technique being identical with that of the first.

Course. The swelling and redness started to diminish following the second treatment, four days later having practically disappeared. On September 16 the lesion was entirely cured. Reexamination on October 21 revealed no evidence of recurrence and no injury to the surrounding tissues.

Summarizing the foregoing, we applied roentgen therapy in a case of chronic dacryocystitis with complete cure. This surprisingly good effect is in sharp contrast to the chronic course which characterizes the lesion without treatment. I believe, therefore, that roentgen therapy as a non-operative procedure is worthy of more extensive use. Careful attention must be paid to the following factors: dose, current amperage, electric pressure, time and interval between treatments. To prevent injury to surrounding tissues a protective lead diaphragm, as in Iizuka's case, must be applied.

In conclusion, I wish to thank Dr. Fujita, our surgeon, and Mr. Yoshida, chief roentgenologist of our hospital, for their kind assistance in preparation of this report.

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THE DETECTION AND ESTIMATION OF RADIUM IN LIVING PERSONS

III.* THE NORMAL ELIMINATION OF RADIUM

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THE question of the normal elimination of radium by persons bearing minute quantities of radium fixed in the bony skeleton naturally assumes importance in connection with any remedial treatment for so-called radium poisoning. Evidently, since the radioactive changes—mainly the expulsion of alpha particles—causing the physiological disturbance cannot be controlled, the objective of remedial measures must be to hasten the elimination of radium and its transformation products. The need of quantitative data expressing the absolute amounts of radioactive products normally eliminated in the excreta is, of course, obvious. Our experiments were undertaken to this end; but this contribution must be regarded merely as a beginning on the problem.

The subjects for these experiments were two girls who had contracted radium poisoning during their employment as dial painters between the years 1917 to 1919. Neither has been exposed to radium in the meantime. The two girls who after a lapse of nearly twelve years are still radioactive, present cases of more than passing interest, inasmuch as they stand as striking examples of the tolerance of living persons to radium.

The immediate object of our experiments was to determine the rate of elimination of radium by these subjects under normal diet and living conditions and thus to deduce for each subject a characteristic individual constant which we may speak of as an "elimination factor," or "coefficient of elimination."

To this end we must know the total quantity of radium present in the subject, as well as the quantity eliminated day by day. According to present knowledge, the radium is contained in and is distributed over the entire bony skeleton, though probably the distribution is not uniform. Its quantitative estimation was carried out (*a*) by making gamma-ray measurements on the subjects by means of a standardized electrometer, and (*b*) by adding to the value thus obtained, the quantity of radium responsible for the radium emanation (radon), found present in the air expired by the subjects.[1] The quantity of radium removed day by day is represented practically entirely by the radium present in the excreta, about 90 per cent being found in the feces. Quantitative determinations of radium were made on the daily excreta collected for a period of a week.

As early as 1915 Seil, Viol, and Gordon[3] conducted some experiments on the elimination of radium by living persons in the feces and urine. In the case of intravenous injection—100 micrograms radium element as chloride—the excreta were assayed for radium over periods of ten days to three weeks immediately following. When 50 micrograms was taken by mouth, the radium determinations were terminated with the sixth day following. Taken by mouth, a much greater part of a soluble radium salt was found to be eliminated during the first three or four days than when introduced intravenously, but after that the rate of elimination was practically the same. These investigators found that the main part of the radium was eliminated in the feces. They report that 25 to 35 per cent of the radium taken by mouth remains in the body four to five days after ingestion. By the tenth day after taking the radium, the daily rate of elimination is

* See references 1 and 2.

less than 1 per cent. This results in an exceedingly slow elimination of the radium remaining, and the authors infer that the process goes on for months. The first rapid elimination of radium evidently takes place before the radium has become "fixed" or deposited in the tissues—mainly in the bones, as we have learned since.

One of us (H. S.) in repeating the experiment of Seil, Viol and Gordon by drinking water containing a known quantity of radium bromide—2 to 5 micrograms—confirmed the rapid elimination of radium in the excreta during the first week after ingestion. In the first experiment it was found, however, that as high as 91 per cent of the radium taken was eliminated during the first four days after drinking the radioactive water. When the experiment was repeated two weeks later, it was found that practically all (98 per cent) of the radium taken was eliminated during the first five days after drinking the radioactive water. In both experiments the presence of radon in the expired air could not be detected after the fourth day.

As already stated, the subjects of our experiments were two girls who had become radioactive twelve years ago. They gave a positive test for radioactivity when examined by the gamma-ray method, and the presence of radon in the expired air was definitely established for each subject. The quantitative determinations by the two methods were conducted daily for a period of five consecutive days. When combined and averaged these determinations give the total radium content for each subject.

Considerable care was exercised in securing the excreta from the subjects. The girls were hospitalized for a week in charge of a special nurse. Since the radium content of the excreta is extremely small the entire feces and urine for a twenty-four hour period were taken for the radium assay. The feces samples were first dehydrated in an oven by gentle heating and finally incinerated to a gray ash. The urine samples were evaporated to dryness and the residue calcined at 800° C. until all carbonaceous matter was burned off. Radium was determined in the residues by two or three of the standard methods[4,5,6]. In most of the determinations the sample was first completely de-emanated by fusing it with potassium bisulfate, or solution in nitric acid. After the lapse of a week or two the emanation which had accumulated in the sealed sample was separated quantitatively, collected, and transferred to the ionization chamber of a calibrated electroscope. From the observed increase in the drift of the charged leaf of the electroscope the small amount of radium present in the sample was then computed. Special care must be

TABLE 1

RADIUM CONTENT OF EXCRETA, SUBJECT A

Date Feb., 1929	Sample Number	Net Weight of Residue (Ash)	Radium Content in Micro-micrograms ($\mu\mu$g.) (10^{-12} g.)	
			Actual	Per Gram of Residue
19	1	0.450	329	730
20	2	2.248	1685	750
21	9	1.778	1067	600
22	10	0.379	274	725
24	12	4.579	2435	530
25	13	1.644	843	514
26	16	1.600	768	480

Total radium in feces ..... 7,403 $\mu\mu$g.
Average daily elimination of radium in feces ..... 1,058 $\mu\mu$g.

exercised in making radium determinations on samples such as these, the radium content of which is extremely small. Blank determinations were made on all reagents used, and the laboratory used was one restricted to measurement of very low grade radioactive preparations.

In Table I are summarized the analytical results obtained for the excreta from Subject A covering a period of a week. A parallel series was determined for Subject B, and the results are recorded in Table II.

There should be added to the above figure the radium present in the urine, which was found to be 103 $\mu\mu$g. as an average of determinations on two samples. The total radium eliminated daily is thus brought up to 1,161 $\mu\mu$g. Since Subject A bears approximately 24 micrograms of radium element, simple division gives the value 5×10^{-5} (0.005 per cent) as the coefficient of daily elimination for this subject.

TABLE II

RADIUM CONTENT OF EXCRETA, SUBJECT B

Date Feb., 1929	Sample Number	Net Weight of Residue (Ash)	Radium Content in Micro-microgram ($\mu\mu$g.) (10^{-12} g.)	
			Actual	Per Gram of Residue
20	3	0.781	347	444
21	4	3.425	459	134
22	11	2.771	301	109
24	14	1.205	115	96
25	15	2.169	215	99
26	17	2.501	409	164

Total radium in feces ..... 1846 $\mu\mu$g.
Average daily elimination of radium in feces ..... 308 $\mu\mu$g.
Daily elimination of radium in urine ..... 55 $\mu\mu$g.
Total radium per day in excreta ..... 363 $\mu\mu$g.
Total radium in system Subject B ..... 14 μg.
Coefficient of elimination, 2.6×10^{-5} daily or 0.0026 per cent per day.

DISCUSSION

In view of the fact that the two subjects studied here had retained radium in their bodies for a number of years, one may readily infer that the rate of elimination must have been very small. These experiments establish this fact and give reasonably close estimates of the rate of elimination for each of the subjects. The results, reported by earlier investigators, that the eliminated radium is found largely in the feces, has been confirmed. The most important result is, however, the marked difference found in the daily rate of elimination of the two subjects—one being 0.005 per cent and the other 0.0026 per cent. It may be well, therefore, to discuss this result somewhat in detail.

The percentage rate of elimination is based on two quantities determined experimentally: (1) the amount of radium in the body, and (2) the amount of radium in the excreta collected over a certain period of time. The first quantity is very difficult to determine accurately in the living subject. In fact, at present, certain assumptions are always involved in any determination—or better, estimation—of the amount of radium in a living subject. The chief difficulty lies in the calibration of the electrometer used for the gamma-ray measurements. The instrument used in the tests reported here was calibrated by a method which has already been described,[1] and a calibration factor was obtained on the assumption that the radium is distributed uniformly throughout the bony skeleton.

As a check on this factor, the following experiment was performed: Twenty to forty standard one microgram ampules of radium solution were distributed over the surface of the body of a normal individual in such a way as to approximate the distribution of the bones in the body. Measurements were then made on this "activated" body in the same way as in the case of the two girls. Since the amount of radium attached to the body in this case was known, it was possible to determine a factor for the experimental set-up which would translate the electrometer readings into micrograms of radium *on* the body. The factor thus obtained was about 40 per cent higher than the one previously obtained by an entirely different method.[1] Considering that the ampules were fastened to the surface of the body, while in the previous calibration the radium was assumed to be in the bones, the discrepancy between the two factors is not unreasonable. It is probable, therefore, that the absolute values of the radium in the bodies of the two girls determined by the gamma-ray method are reasonably correct.

However, the problem is further complicated by the fact that Subject B carries mesothorium as well as radium. The radioactivity of Subject A is due to radium alone. The presence of mesothorium in Subject B was established definitely by showing the presence of thorium emanation, thoron, in the expired air. The actual quantity of mesothorium, expressed as radium equivalent, must be relatively very small, for in the first place the test for thoron in expired air is far more sensitive than the detection of radon; secondly, since the half life period of mesothorium is only, approximately, seven years, as against 1,600 years for radium, it is evident that in the course of twelve to thirteen years most of the mesothorium originally present has decayed. At best not more than 25 per cent of the initial quantity present would now remain, even if there had been no elimination of mesothorium. We are thus led to conclude that the activity of Subject B is to be ascribed to radium almost entirely.

The total amount of radium in the body is made up of two parts: (1) the amount which retains radon and its subsequent products (Ra A, B, C), and (2) the amount which is freely emanating and does not retain the radon produced. The gamma-ray measurements made with the Wulff-Hess instrument can determine only the first part. The second part can be estimated by measuring the amount of radon in the expired air. To do this it is necessary, of course, to measure the volume of air expired in normal breathing in a given interval of time. The expired air tests were made in two ways: (1) the subject was asked to blow through a drying train and an ionization chamber for a time sufficiently long to make sure that practically all the air originally in the chamber had been replaced by "expired air." (2) The subject was asked to blow directly into a Douglas bag, without a drying train, to insure more normal breathing. This air was then passed through a drying system and through the ionization chamber. The air collected by the second method was always found to be less active than expired air forced directly into the chamber by the subject under test. The lower values were given more weight in computing the amount of radium which liberated the radon present in the expired air. Combining all the experimental results, we may say that the most probable values of the radium content of the two subjects are:

Subject A 12.6 μg. non-emanating 11.4 μg. emanating = 24 μg.

Subject B 12 μg. non-emanating 2 μg. emanating = 14 μg.

These figures were used in calculating the percentage rate of elimination of radium from the system.

It is important to note that the same procedure was employed, and the same assumptions were involved, in the determinations of the total radium content of the two subjects. Therefore, the ratio of the two totals cannot be influenced greatly by the ac-

curacy of the absolute magnitudes of the two. In other words, even if the actual amounts of radium in the two subjects are quite different from the values given above, their relative values cannot be very different. (If the assumption of even distribution of radium in the bones is correct.) The same thing applies to the second quantity involved in the calculation of the per cent elimination rate, i.e., the amount of radium in the excreta collected over a definite period. The amounts of radium to be measured in both cases were very small, but they were of the same order of magnitude and the same experimental procedure was used. Accordingly, their *relative* values would not be influenced considerably by the absolute values of the radium content of the residues. *On this basis* one may conclude, therefore, that the *difference* in the percentage elimination rates in the two cases is significant, irrespective of the absolute values of the quantities involved. As already stated, the two rates are: Subject A, 0.005 per cent per day; Subject B, 0.0026 per cent per day. Hence, Subject A is eliminating radium about twice as rapidly as Subject B. Taking into account the larger amount of radium present in Subject A we find that per day she is eliminating about three times as much radium as Subject B (1,161 as compared with 363 $\mu\mu$g.)

In the absence of any definite information as to the mechanism of radium "fixation" in the body and subsequent gradual elimination, it is very difficult to account for the experimental results. We may, however, use these results for "speculative" purposes in an attempt to analyze the problem more closely. Let us consider first the difference in the percentage elimination rates. As already stated, the determination of the amount of non-emanating radium present in the body is based on the assumption that the radium is evenly distributed throughout the bony system. If this is not actually the case but the radium is concentrated largely in some bones, the relative amounts present in the two subjects may very well be quite different from those calculated above. For instance, if we assume that the radium in Subject B was more effective on the electrometer because it was largely concentrated in a bone near the instrument, the calculated amount was greater than it should have been, in comparison with the amount measured in Subject A where this condition did not obtain. If the amount of non-emanating radium actually present in Subject B was about one-half of the amount indicated by the gamma-ray measurement, the percentage rate of elimination would be practically the same for both subjects (about 0.005 per cent per day).

We may summarize these results as follows: (1) If we assume that the radium is evenly distributed throughout the bony system, the experimental results lead to the conclusion that the percentage rate of elimination is quite different for the two subjects. (2) If we assume that the percentage rate of elimination should be the same for both, then the radium cannot be evenly distributed throughout the bones in both subjects. There is not enough well-established experimental information to enable us to decide between these two assumptions. So far, most workers in this field are of the opinion that the radium is fairly evenly distributed throughout the bones. However, the fact that at least some girls show localized bone lesions, lends strength to the suggestion that probably the radium is more or less concentrated in some bones, although the whole bony system is infiltrated with radium to a certain extent. Evidently more and better experimental evidence is required before any definite conclusions can be drawn. To this end we may suggest the following experiments: (1) To determine the radium content per gram of bone with specimens obtained from widely separated parts of the same body. (2) To make gamma-ray tests on two subjects with the instrument placed successively at the level of the neck, pelvis and knees, as well as opposite the most important bone lesion, in both cases. In this ex-

periment, if the radium is evenly distributed in the bones, the readings for any two corresponding positions of the electrometer should be essentially in the same ratio.

We have in hand a few experimental data which indicate that the radium present in the bony skeleton of persons who are radioactive is not approximately uniform in distribution as is generally assumed, but our experiments have not gone far enough to permit us to draw a definite conclusion. For example, in making gamma-ray measurements on a living subject the readings were made with the instrument placed in positions other than the conventional one: (*a*) When the electrometer was placed near the side of the face opposite the jaw bone, which had formerly shown signs of incipient necrosis, the radium content for the entire body, based on the electrometer reading, was found to be 14 μg.; (*b*) a reading made with the instrument opposite the ankle gave a value of 9 μg.; (*c*) with the instrument in the normal position, opposite the middle of the back, the value for the total radium content was 11.6μg. Apparently the higher value obtained when the instrument was near the face indicates a local concentration of radium in the maxillary bones. But an isolated case like this does not prove the point.

Another bit of experimental evidence gives a more definite indication. In a series of quantitative determinations of radium in specimens of bone from a radioactive skeleton, the radium content of the humerus averaged 2.67×10^{-9} g. radium per gram of air dry bone. For a specimen of rib the value found was 3.4×10^{-9} g. radium per gram. A specimen of vertebra showed a still higher value of 5.2×10^{-9} g. radium per gram of bone. Moreover, when the values are computed to radiun content of bone dried at 110° C., or to bone ash, the relative values for the radium content per gram do not change materially.

It may be well to consider further the possible significance of the difference, or equality, in the percentage rate of elimination for the two cases. Subject A eliminates per day about three times as much radium as Subject B. If we assume that the same percentage rate of elimination applies to both, then Subject A must contain about three times as much radium as Subject B. This is probably a reasonable conclusion for the processes of radium "fixation" and elimination must be essentially the same in both cases. It is pretty well-established that most of the radium in these cases is in the bones (very little or none has been found in the soft tissues). The two girls worked under similar conditions, ingested radioactive material slowly, and have had radium in their bodies for twelve or more years. Therefore, the radium should be in substantially the same chemical and physical state in the two cases.

Considering now the separate components of non-emanating and emanating radium estimated experimentally we have: (1) In Subject A, $11.4/24=48$ per cent of the total amount of radium is in the emanating form. (2) In Subject B, only $2/14=14$ per cent is in this form. If these results are accepted, then the radium cannot be in the same chemical and physical state in both subjects, which is contrary to what one might expect. Here again if the amounts of non-emanating radium determined by the gamma-ray method are incorrect on account of uneven distribution in the bones, the difference is not significant. In fact, the two can be brought closer by suitable changes in the values for the non-emanating radium. Furthermore, these changes are consistent with the requirement mentioned above that Subject A should contain about three times as much radium as Subject B.

On the other hand, if we accept the idea that the radium is not in the same chemical and physical state in the two cases, we can account for the greater rate of elimination of Subject A on the basis that a much larger proportion of the radium in her body is in the emanating form. It may be also that elimination becomes slower, the smaller the total amount of radium present in the body. In this case one might expect that

after a certain minimum amount of radium has been reached, elimination will be extremely slow or cease entirely. In the subjects under consideration the rate of elimination is very small but it is still measurable. In view of the long time which has elapsed between the ingestion of radium and these tests, one may expect that radium will continue to be eliminated in these patients for a long time. At the present rates, it will take Subject A about two and one-half years and Subject B twice as long to eliminate 1 microgram of radium. These estimates, of course, are tentative and are subject to modifications according to the possibilities discussed above.

It may be of some interest to note that in Subject A the amount of radium found in the urine was 9 per cent of the total eliminated per day, whereas in Subject B it was 15 per cent. However, such differences lie within the limits of experimental errors, since the actual quantity of radium in the urine residues is not only very small but is relatively small in comparison with the radium content of feces residues. Similarly the variations in the radium content per gram of residue of the feces (see last column of Tables I and II) are probably of little significance. They emphasize, however, the importance of an extended period of observation in any experiments of the type described here.

Finally, we wish to suggest that the observed difference in the normal rate of elimination of radium by these subjects is probably based upon a physiological factor, a marked difference in the rate of metabolism of the subjects. Subject A expires 1 liter of air in eight seconds; Subject B, 1 liter in fourteen seconds; Subject A breathes normally once in 4.2 seconds; Subject B, once in 2.85 seconds. This fact, together with the observation that Subject A leads a more active life than Subject B, points to a higher plane of metabolism on the part of Subject A, which might favor the more rapid rate of elimination of radium observed for Subject A. In other words, the "coefficient of elimination" is probably a specific factor for the individual, closely associated with physiological function.

From the preceding discussion it is evident that no very definite conclusions may be drawn from our work and the available information on this subject. However, it is evident that the idea that radium is distributed uniformly throughout the bony system in "radium poisoning" cases, needs to be checked carefully. The experiments do show definitely that radium continues to be eliminated from these cases even twelve years after ingestion of the material, although the rate of elimination is very small. They also show that most of the radium eliminated daily is found in the feces. We hope that our experimental results and the discussion of some important factors involved in the problem, will be of some use to those who have occasion to make radioactive measurements on "radium poisoning" cases, and to those who are devising therapeutic means for ameliorating the condition of these patients.

The work presented in this paper was undertaken at the suggestion of the Medical Commission in charge of the patients. The Wulff-Hess electrometer used for the gamma-ray tests was loaned by the United States Radium Corporation. The authors wish to express their appreciation of the spirit of cooperation exhibited by the Commission and the patients throughout the course of the experiments.

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ULTRAVIOLET MEASUREMENT WITH THE CADMIUM PHOTO-ELECTRIC CELL

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THE advantages of the cadmium vacuum photoelectric cell for ultraviolet measurement have been pointed out repeatedly.[1] Briefly the chief advantage lies in its insensitivity to visible light dispensing with the filters necessary with potassium and sodium cells. A further advantage comes from the fact that the dependence of sensitivity of a cadmium cell with a heliol filter upon wave length closely approaches the dependence of erythema effectiveness upon wave length.[5] The vacuum cadmium cell has inherent advantages over the gas cell. Chief among these is the stability of the vacuum cell and the fact that the photo-electric current is independent of applied voltage once the saturation voltage is exceeded.

The principal disadvantage of the cadmium vacuum cell lies in the smallness of the photo-electric current. This current is many times less than the current produced in a gas cell for the same illumination. It is, in fact, so small that electroscopic methods have been used for its measurement.[4] Such methods have the disadvantage of requiring an appreciable time for a reading, which is taken by timing the passage of an indicator across a scale. Direct instantaneous readings may of course be made with a very sensitive galvanometer with all the difficulties inherent in the use of such an instrument. The present paper is a description of a method of taking instantaneous readings with essentially very rugged apparatus.

Pohle and Huxford[3] have reported an arrangement containing a vacuum tube amplifier. The indicating device used by them is a microammeter. This is of course a step forward toward the desired ruggedness but a microammeter is still a rather delicate and expensive instrument. It is possible to modify Pohle and Huxford's circuit by the addition of a stage of power amplification so that the indicating meter is a milliammeter, a very rugged and relatively inexpensive instrument.

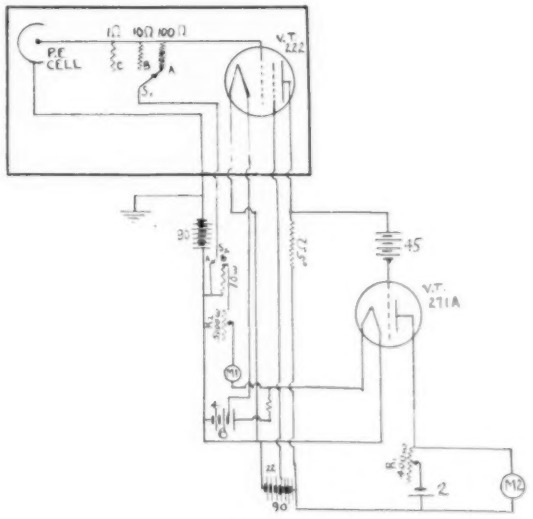

FIG. 1.

The circuit is indicated in Figure 1. The first stage of amplification is obtained with a screen grid tube because of its high amplification factor and because of the highly insulated grid which enables the grid voltage to follow the voltage drop across very high resistances, and thus to control the plate voltage of the tube with a minimum of power. The power stage consists of a 271 A tube which has a comparatively high mutual conductance and so yields large plate current changes for small grid voltage changes. This tube also has a relatively long straight characteristic.*

The circuit was designed with an eye to practical dimensions. For this reason the

* The use of the 231 tube, a type which was put on sale after the submission of this report, would seem to constitute an improvement.

plate voltage on the first tube is low as compared with its normal rating when working into a plate resistance as high as that here used (0.5 megohm). This low voltage and high resistance has the advantage of yielding a very low steady plate current so that the plate batteries remain constant over long periods. The same reasoning prompted the low voltage on the plate of the power tube.

The device is divided into two sections. The first part is separated on the diagram by the rectangle (upper left). The apparatus so separated consists of the cadmium cell itself, the voltage amplifying tube, the necessary grid resistors and connecting devices. This apparatus is housed in a grounded metal box and connected by means of a flexible shielded cable to the remaining apparatus, inclusive of batteries, mounted on a rolling table.

The photo-electric cell is mounted in the grounded box with an adjustable diaphragm and a shutter. Readings are taken by means of the two milliammeters M1 and M2. M1 has a full scale of 10 milliamperes, M2 shows maximum deflection with 1 ma.

The operation of the device is as follows: After connecting the batteries by means of switches not shown in the diagram, with switch S2 on A, rheostat R1 is adjusted until meter M2 reads full scale (1 ma.). In this way the steady plate current of the power tube has been compensated. Then switch S2 is switched to B, and rheostat R2 adjusted until meter M2 reads zero. The reading of M1 is then an indication of the amount of voltage on the grid of the voltage amplifier necessary to give full scale deflection of M2. With S1 connected to one of the three resistors the photo cell may be exposed to the radiation to be measured. A deflection will be produced on M2 and the photo-electric current is given by

$$\frac{M_1 M_2}{100R} \text{ microamperes}$$

where M1 and M2 are the readings of the two meters in milliamperes and R is the resistance of the grid resistor A, B, or C in use, in megohms.*

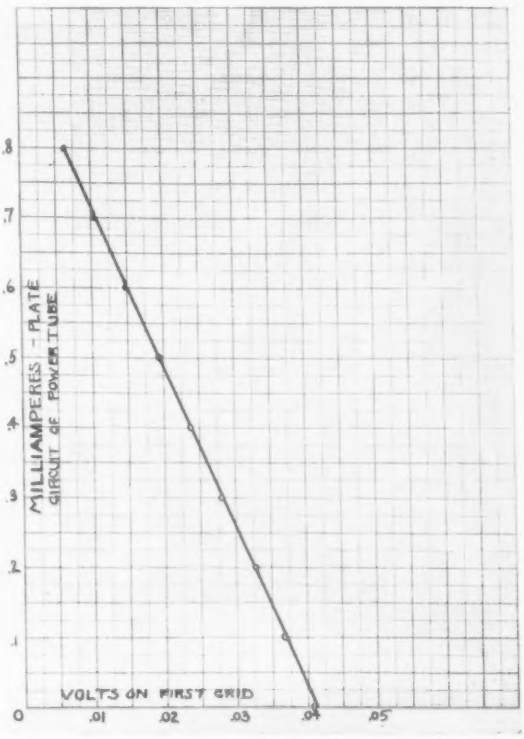

Fig. 2.

The justification for this simple formula and the lack of a calibration curve lies in the fact that, because of the high net mutual conductance of this system, only very small actuating voltages are required, so that if M2 is not off scale, the two tubes are operating on only a very short straight section of their characteristics. Figure 2 shows the net characteristic of the system over the range in question. The circles are observed values, while the line is a straight line drawn with a straight edge. The net mutual conductance of the system is 23,000 micromhos, while that of the power tube alone is about 1,000 micromhos, showing that the effective voltage amplification of the first tube is about 20. While these values may change from time to time due

* The general expression for the current in amperes is M_1R_1X/R where M_1 is the reading of M_1 in amperes necessary to reduce M_2 to zero with no photo current and S_2 at B, R_1 is the resistance at point B of switch S_2 (10 ohms in this case), X is the ratio of the readings of M_2 with switch S_2 at A without photo current to that with switch S_2 at B with photo current, R is the resisance of A, B or C in ohms.

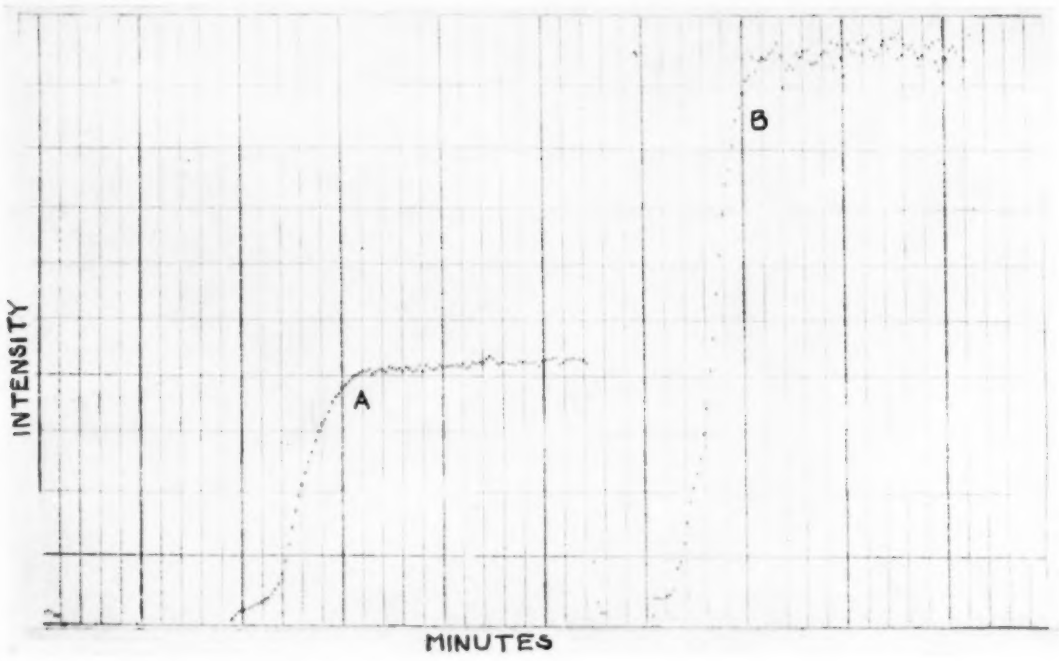

Fig. 3.

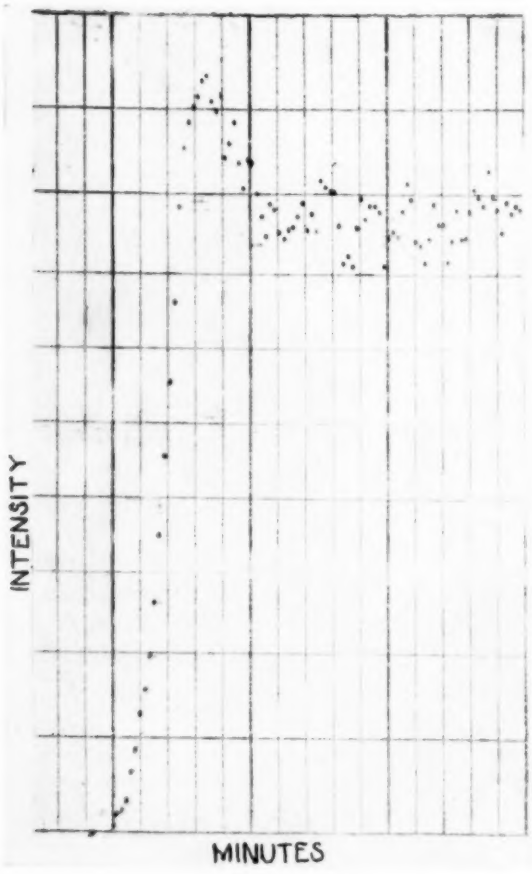

Fig. 4.

to battery, filament and other changes, the straightness of the characteristic should not change. It is only the linearity and not the absolute values of the characteristic which enter into the expression for the current given above.

Instead of balancing the static plate current of the power tube in the manner indicated, i.e. with the help of an auxiliary battery, other methods were tried, particularly the bridge method proposed by Williams, Eglin[5] and others. For the purpose in hand the additional complications were found to be unnecessary. The zero drift with heavy duty B batteries for the high voltages and storage cells for the low voltages is sufficiently small to be of no importance after a steadying period of from fifteen to thirty minutes.

The sensitivity of the device is so great that for ordinary measurements with a quartz mercury burner the one megohm grid resistor was found to be too high and in use the diaphragm is stopped down. With the heliol filter over the cell the same burners require resistors of 10 to 100 megohms to give a reasonable deflection. The sensitivity may be increased tremendously,

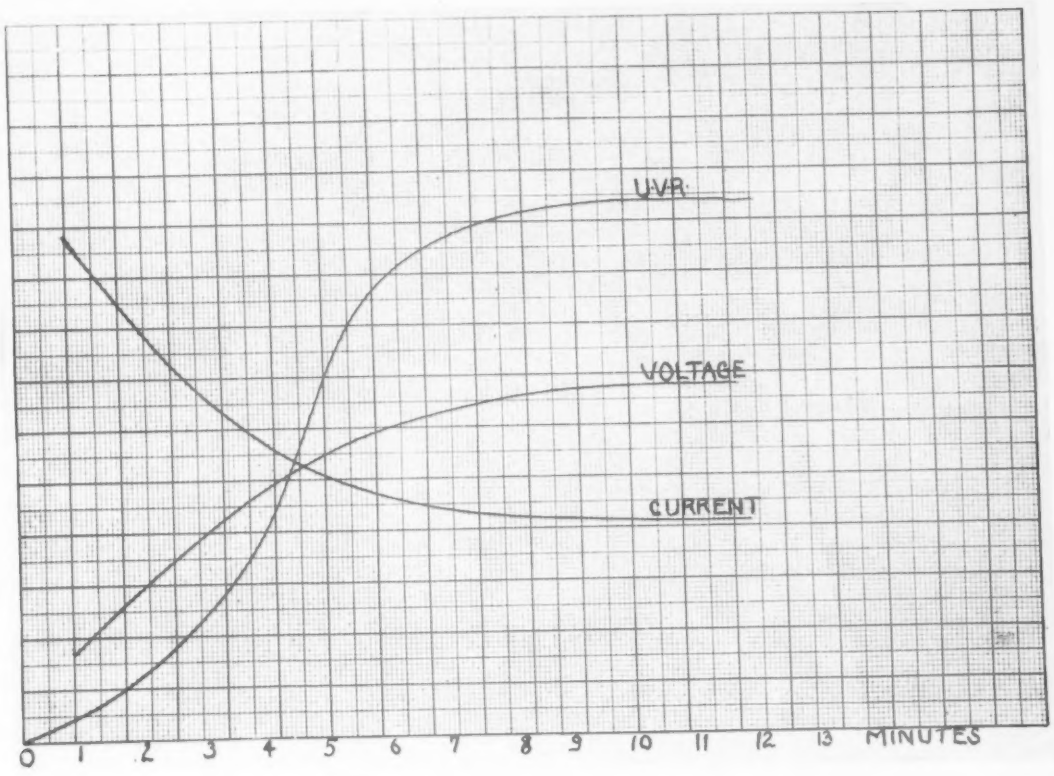

Fig. 5.

at the expense of accuracy and duplicability, if switch S1 is left entirely open.

Instead of using an ordinary milliammeter for M2, a recording instrument may be substituted. Records so taken of the starting of a Hanovia and a G. E. burner are shown in Figures 3 and 4. A of Figure 3 is the record of the starting of the Hanovia burner, B of the G. E. burner. The relative heights are of little importance as the latter burner was a new one kindly loaned by the General Electric X-Ray Corporation while the former was an old much used burner. Figure 4 represents the starting of a G. E. burner with a different value for the burner resistance in series with it. The high initial peak prior to stabilization is noteworthy. This peculiarity of the arc with certain burner resistances could only have been followed with great difficulty by electroscopic or chemical methods.

Figure 5 represents the entire starting characteristics showing the growth of ultraviolet radiation and voltage and the corresponding drop in current.

SUMMARY

A two-stage amplifier is described for use with the vacuum cadmium photoelectric cell. It has a straight line characteristic over the entire useful range and its indications may be interpreted directly in terms of photo current. Because of the nature of the circuit slight changes in batteries or tubes are compensated.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Thirty-second Annual Meeting: Haddon Hall, Atlantic City, N. J., September 22–25, 1931.

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Seventeenth Annual Meeting: 1932, to be announced.

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EDITORIALS

THE ANNUAL MEETING

THE annual meeting of the American Roentgen Ray Society, the thirty-second in its history, will be held at Atlantic City, N. J., from September 22 to 25, 1931.

Haddon Hall has been chosen as the headquarters and there all meetings and exhibits will be held.

The choice of Atlantic City as a meeting place is a fortunate one, both on account of its accessibility and also on account of the hotel facilities which it offers. Haddon Hall where the meeting will be held has accommodations for the meeting room, the scientific and commercial exhibits on the same floor, which is the fourteenth, thus obviating the unpleasantness of outside noises and assuring perfect ventilation.

Aside from the physical arrangements which have been made, the scientific program which Dr. Jaches, the president-elect, has prepared is an unusually comprehensive one. While no special effort on his part has been made to have symposiums on special subjects, the papers that will be given tend to group themselves. As an indication of the extent and scope of the papers to be read, it is only necessary to consult the complete program which is published in this issue.

The Caldwell Lecture which is always a feature of the annual meeting is to be given this year by Dr. Fedor Haenisch of Hamburg, Germany, and the Society is fortunate also in having as guests Dr. Coutard of the Radium Institute of Paris, who will read a paper on "Roentgen therapy of the epitheliomas of the tonsil, larynx and hypopharynx—1920–1926," and Dr. Elis Berven of Stockholm, Sweden, who will read a paper on "Development of Technique and Results in the Treatment of Tumors in the Nasal and Oral Cavities."

Dr. Jaches is to be complimented on the high quality of the program which he has arranged for the meeting. The program in its variety of subjects should make a widespread appeal and we anticipate a large attendance at the meeting.

The scientific exhibit, under the direction of Dr. Pendergrass, promises to be a very complete and comprehensive one. In order to enhance the value of the exhibits time will be allotted during the day for the inspection and demonstration of the various exhibits. This is a feature which has been somewhat neglected in the past and the Scientific Exhibit Committee feeling, as others have this neglect, have made arrangements for a more personal demonstration of the exhibits.

Another feature of the meeting which is always interesting and instructive is the commercial exhibit where the manufacturers have on display the more advanced ideas in construction of apparatus and accessories. These exhibits are brought to the meeting at considerable cost and effort on the part of the manufacturers and we would recommend that all those attending the meeting avail themselves of the opportunity to inspect in detail the various exhibits.

Aldred Scott Warthin

1866–1931

ALDRED SCOTT WARTHIN

1866 – 1931

TO ALDRED SCOTT WARTHIN, Pathology was much more than a narrowly conceived recognition of the effects of disease processes as discovered by the gross and microscopical inspection of organs and tissues. For him Pathology illumined the entire field of Medicine and his interests were broadly clinical as a result. He had, too, an extraordinary interest in the possible application of newly discovered agents in the production of disease and in their possible curative effects. It was this vision, this ability to foresee the future significance of things, which led him to inaugurate intensive studies in the pathology of mustard gas poisoning long before the large scale production of that substance was possible in this country. Similarly, he interested himself very early in the effects of roentgen rays upon body tissues, both from the standpoint of pathological lesions which might be produced and also as to the possibility of inducing beneficial changes in already diseased tissues by the application of this new manifestation of energy. In 1907 he brought out three studies in this field. One was a comparison of the value of roentgen irradiation and the administration of arsenic in the treatment of leukemia; another was an experimental study of the effects of roentgen rays upon the blood-forming organs, and a third described the effects produced in the kidney by irradiation. In 1913 he reported a case of fatal hemorrhage from the spleen after prolonged radiotherapy and in the following year described in detail the minute changes produced in leukemic tissues by exposure to roentgen rays, a study which was reprinted in both German and French periodicals. More recently further researches, some the result of joint authorship with Case and with Pohle, have dealt with the effects of intensive deep roentgen irradiation upon the liver, the reticulo-endothelial system and the heart. To this large extent, roentgenologists could count Dr. Warthin as one with themselves in investigative work.

Had he accomplished no more in research than his work on the pathology of irradiation we would have been fully justified in honoring the memory of Dr. Warthin. But the titles listed above are only a small fraction of the hundreds which bespeak his extraordinary energy, industry and breadth of interests. Tuberculosis of the placenta; the histology and pathology of the hemolymph nodes; the genetic unity of that entire group which includes the leukemias, Hodgkin's disease, chloroma, myeloma and lymphosarcoma; traumatic lipemia; the pathology of the Pacinian corpuscle; the thymico-lymphatic constitution; the neoplastic constitution, and the Graves' constitution were among the major topics upon which he wrote. It was for his work upon the pathology of syphilis, however, that Dr. Warthin was best known. Becoming interested at first in the lesions of congenital syphilis, he early recognized the essential unity of the pathology of syphilis as found in various organs and as manifested in various stages of the disease. In a series of about forty papers he developed a new conception of the pathology of late, and of latent, syphilis, particularly as it appears in the aorta, heart, testes, pancreas and adrenals. In the course of this investigation new methods for staining the causal organism were devised and it was successfully demonstrated in lesions in which it had never before been seen.

Aldred Scott Warthin was born at Greensburg, Indiana, October 21st, 1866, and died at Ann Arbor, Michigan, May 23rd, 1931. His early inclination was toward music and he received a Teacher's Diploma in Music from the Cincinnati Conservatory in 1877. He obtained the A.B. degree from the University of Indiana in 1888;

A.M. from the University of Michigan in 1890, and M.D. and Ph.D. from the latter in 1891 and 1893 respectively. He was married to Katherine Angell in 1900 and to them four children were born. As a teacher and investigator Dr. Warthin served from 1891 to 1895 under Dr. George Dock in the Department of Internal Medicine at the University of Michigan, first as Assistant and later as Demonstrator in that department. He was made Demonstrator of Pathology in 1896; Instructor, 1897; Assistant Professor, 1899; Junior Professor, 1902, and Professor and Director of the Pathological Laboratories in 1903, holding this position until his death.

Dr. Warthin held membership in many scientific societies in the fields of Medical Biology, Pathology and Internal Medicine. Many of these organizations he serves as president: the American Association of Pathologists and Bacteriologists in 1908, the International Association of Medical Museums from 1910 to 1913, the American Society for Experimental Pathology in 1924, the American Association for Cancer Research in 1928, the Association of American Physicians also in 1928, and the American Association of the History of Medicine in 1930–31. To each of these organizations he gave most freely of his time and energy.

Unusually gifted in public address, Dr. Warthin was in constant demand as a speaker at medical gatherings and he was ever generous in respect to such requests, accepting invitations to the full limit of his time and strength. His vivacious, dynamic and compelling manner in speaking, typical of all of his activities, made his presentations effective, and to some who were not aware of the accumulated evidence which supported them, his pronouncements seemed dogmatic.

In literary presentation he was equally successful for Dr. Warthin wrote with ease, clarity and artistic style. While these qualities were present from the first in strictly medical papers, they became more evident in such historical essays as "*An American Medical Student*"; in the many editorials, all of which he wrote himself during the six years in which he was Editor of the Annals of Clinical Medicine, and particularly in the three books which appeared in the last three years of his life—"*Old Age*," "*The Creed of a Biologist*," and "*The Physician of the Dance of Death*."

To one who had brought honor so abundantly upon the institution which he represented, honor was also due and was paid in no small degree. The University of Indiana granted Dr. Warthin an honorary LL.D. in 1928, forty years after his graduation. Another token of recognition which meant much to him was the Festschrift presented to him at his sixtieth birthday, when he had completed thirty-five years of teaching in the University of Michigan. In this collection of original papers, covering a wide range of medical subjects, are to be found contributions from one or more members of each of the thirty-five classes to which Dr. Warthin had then taught Pathology.

With interests as broad as life itself, with unusual aptitude and special training in diverse fields—music, art, biology and gardening, as well as Medicine, with a rare sympathy towards the problems of human life, Aldred Scott Warthin made a profound impression upon those who sat before him as student and upon those who learned to know him outside of the classroom. He was a hard taskmaster, but required no more of others than of himself, and the high standards in respect to both quantity and quality of achievement which his students were required to meet, meant that much more in enrichment of their intellectual material. He taught them how to observe and to think for themselves. He was characterized by untiring energy, broad culture, personal fastidiousness and unswerving loyalty to his friends and to his chosen interests. A warm and mellow philosophy colored his later years, a "philosophy of life which has animated and directed my existence, which has given meaning to the Universe for me, and brought me peace of mind and happiness." (From the Foreword of *The Creed of a Biologist*.)

Carl Vernon Weller

CHARLES ALLEN PORTER

BY THE DEATH of Dr. Charles Allen Porter, late Surgeon to the Massachusetts General Hospital, the American Roentgen Ray Society has lost an honorary member who, although a surgeon of distinction, was allied to the development of American Roentgenology by bonds peculiarly intimate. This association was engendered of his long professional care of the late Dr. Walter James Dodd—a care that was singularly meticulous and entwined with a close friendship that became ever augmented with the years.

Doctor Porter represented the eighth generation of a family line of physicians extending unbroken from the life of Dr. Daniel Porter (1625–1690) of Farmington, Connecticut, spanning chronologically the entire history of New England, and now terminated with this recent death. His father, Dr. Charles Burnham Porter (1840–1909), was a distinguished member of the Staff of the Massachusetts General Hospital and whose mantle as a surgeon as well as a teacher at the Harvard Medical School, fell upon the worthy and extraordinarily energetic shoulders of the son.

The immediate results of Doctor Porter's surgical care of the case of Doctor Dodd, roentgenologist to the Massachusetts General Hospital, brought to his door from far afield many who had become similarly afflicted and, while there have been some in whom his efforts could result in little but palliation, there are many others who owe to him their present tenure of life.

Although a definite contributor to the surgical literature, Doctor Porter needed urging to speak publicly of his own accomplishments but, through the efforts of President Caldwell, he was persuaded to describe, in a paper read at the New York meeting of 1908, his results in the surgical treatment of the late and severe manifestations of roentgen-dermatitis up to that time, with especial reference to skin-grafting. A second communication appeared later.

When a medical man becomes a teacher, he lays himself open to the judgment of his students and it is usually of his personality rather than of his erudition that the first mass-opinion is formed, and it is a remarkably correct one in most instances. As a teacher, Doctor Porter was so vigorously specific in his methods that a conviction as to his calibre as an instructor was automatically established, while the soubriquet of "Allie Porter" was so generally and spontaneously adopted by pupils and associates alike that the impulse could come only from hearts caught up in the wave of his enthusiasm and forthwith enmeshed in the loyal bonds of affection.

A reminiscent mind will ever recall the apparent lightness of manner, amounting almost to gaiety, with which he masked his deeper emotion when dealing, as a surgeon, with patients who were medical men, of whom he had so many among those impaired by the untoward effects of irradiation. On a point of diagnosis, his pronouncement of "carcinoma" could be expressed in a manner that seemed to make of it well-nigh a pleasantry. Surgeon and patient both knew it, so why not play the philosopher? In spite of this he never allowed a false impression to be created. One pair of eyes has more than once noted the quick sobering of his face when he thought those eyes were not upon him.

"Allie" Porter, in his surgical warfare against the progressive ravages of profound x-ray burn, usually had a tough opponent in front of a sector onto which he had been brought up only after the resistant forces had become deeply entrenched, whereby he could not always attain his objective. Each new demand upon his skill, however, brought forth reinforcements of enthusiastic energy from sources apparently inexhaustible. Of his brilliant successes, impossible for one of less experience in this field of distinctive pathologic phenomena, he spoke little in casual discussion. It remains for the fortunate beneficiaries of his proficiency to recount them, and to carry, in gratitude, the memory of his ministration and his friendship down the gentle gradient from Life's plateau.

PERCY BROWN

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. John T. Murphy, 421 Michigan St., Toledo, Ohio.
Thirty-second annual meeting: Haddon Hall, Atlantic City, N. J., Sept. 22-25, 1931.

American College of Radiology
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual Meeting: New Orleans, La., 1932.

Section on Radiology, American Medical Association
Secretary, Dr. G. W. Grier, Jenkins Arcade, Pittsburgh, Pa.
Annual meeting: New Orleans, La., 1932.

Radiological Society of North America
Secretary, Dr. I. S. Trostler, 812 Marshall Field Annex, Chicago, Ill.
Seventeenth annual session: Hotel Jefferson, St. Louis, Mo., Nov. 30–Dec. 4, 1931.

Radiological Section, Los Angeles County Medical Society
Secretary, Dr. John F. Chapman, 209 Professional Bldg., Pasadena, Calif.
Meets on the third Wednesday of each month at the California Hospital.

Radiological Section, Southern Medical Association
Secretary, Dr. W. S. Lawrence, Medical Arts Bldg., Memphis, Tenn.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Masterson, 401-76th St., Brooklyn, N.Y.
Meets monthly on the first Tuesday from October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St.
Meets second Monday of each month except during the summer months, the place of meeting to be selected by the host.

Chicago Roentgen Society
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting second Thursday of each month October to May inclusive at Virginia Hotel.

Cleveland Radiological Society
Secretary, Dr. A. Srauss, 518 Medical Arts Bldg.
Meetings are held at 6:15 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Illinois Radiological Society
Secretary, Dr. Fauntleroy Flinn, 220 South Webster St., Decatur, Ill.
Regular meetings held quarterly.

Indiana Roentgen Society
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

Milwaukee Roentgen Ray Society
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee.
Meets first Friday in October, December, February and April.
Place of meeting designated by the president.

Minnesota Radiological Society
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.
Next meeting: Rochester, Minn., October, 1931

New England Roentgen Ray Society
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

New York Roentgen Society
Secretary, Dr. J. Bennett Edwards, Englewood Hospital, Englewood, N. J.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

Central New York Roentgen Ray Society
Secretary, Dr. Robert C. Hall, 258 Genesee St., Utica, N.Y.
Three meetings a year—January, May and November.

Pennsylvania Radiological Society
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Next meeting, to be announced.

Philadelphia Roentgen Ray Society
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 p.m., in Thomson Hall, College of Physicians, 19 S. 22d St.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave.
Meets monthly on the first Friday evening at 7:45 at the Rochester Medical Association Building.

St. Louis Roentgen Club
Secretary-Treasurer, Dr. E. W. Spinzig, 316 Metropolitan Bldg.
Meets first week of each month. Time and place of meetings designated by president.

Texas Radiological Society
Secretary-Treasurer, Dr. C. F. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Roentgen Ray Society
Secretary, Dr. B. D. Harrington, University Hospital, Ann Arbor, Mich.
Meets every Wednesday evening from October to June, at 7:30 o'clock in the amphitheatre of the University Hospital.

* Secretaries of societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburg, Va.
Next meeting, to be announced.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale.
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Roentgengesellschaft
Meets annualy in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Nicolae Busila, 44 Elizabeta Blvd., Bucarest.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Secretary, Professor Holzknecht, Vienna, IX, General Hospital.
Meets first Tuesday each month, October to July.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto, Japan. Meets bi-monthly on third Sunday.

ATLANTIC CITY

This Year's Meeting Place

Of Atlantic City, where the annual meeting of The American Roentgen Ray Society will be held in September, it has been said that there is no other city which so completely meets the requirements of conventions. The stage is all set for one of the biggest and best gatherings in the history of the organization—a meeting which should go down in history not only from the point of view of attendance, but also for the amount of constructive work accomplished.

The sessions will be held in the beautiful new Haddon Hall, which meets the most exacting demands from the standpoint of comfort, elegance and service.

This convention city by the sea not only lends itself ideally to convention purposes, but it is also one of the wonder spots of the entire world for vacationists. Known from coast to coast, and almost equally well abroad, its ocean-crested shores are a mecca for pleasure seekers. There is probably no time of the year when Atlantic City has more to offer than in September, when the sun still shines down warmly, but the breezes have a touch of freshness to them, making it comfortable for the sessions and extremely pleasant for recreation purposes.

Haddon Hall

Due largely to the many advantages of Atlantic City, a record-breaking attendance is anticipated at this year's meeting, for few members will care to miss this opportunity to enjoy a combination vacation and educational trip to the Nation's most famous playground. Those from the inland

Beach Scene

Boardwalk

will find the beautiful waters of the Atlantic Ocean, just outside the hotel windows, a never-ending source of delight.

Frequent trains, unsurpassed for comfort, speed and safety, are operated to and from New York City via the Pennsylvania and the New Jersey Central Reading Lines

Boardwalk and Beach

and to and from Philadelphia via the Pennsylvania and Reading Lines, connecting conveniently at New York City and Philadelphia with fast through trains from all sections of the United States and Canada.

Architecturally beautiful, Atlantic City hotels rise majestically from the ocean's edge facing a panorama of kaleidoscopic beauty—distant yachts, with full-blown sails silhouetted against an azure sky; a variety of seasonal beach activities along the fringe of tumbling surf, and the always sparkling life of the Boardwalk—a sight that never fails to charm even the most sophisticated world traveler.

Rivaling the most brilliantly illuminated thoroughfares of the world, the Boardwalk and the great piers which stretch seaward are outlined at night with myriads of electric lights, producing an effect of thrilling beauty. To many persons, a stroll on the Boardwalk is, in itself, a most fascinating recreation and diversion. None of the other well-known promenades of the world provide the vivacity and sprightliness of scene and action that fill and charm the eye as one beholds the smartly attired Boardwalk throngs.

Inseparably associated with the life of the Boardwalk are the roller chairs. For unique diversion and charm, few experiences compare with that of relaxing in a roller chair and leisurely enjoying the changing spectacle along this famous marine esplanade.

Atlantic City, of itself, offers many and varied attractions—so many, in fact, that the average visitor is perplexed not so much with "What shall we do?" as with "Which shall we do?" In this great pleasure resort there is a diversity and abundance of recreation and entertainment. The latest and best in stage productions, motion pictures and vaudeville; the many and varied attractions and activities of the Boardwalk and the beach, music and dancing in the hotels and cafes, seemingly unlimited choice of wholesome, pleasant entertainment.

All told—this should be the convention of conventions, so make your preparations now.

PRELIMINARY PROGRAM

OF THE

THIRTY-SECOND ANNUAL MEETING

OF THE

AMERICAN ROENTGEN RAY SOCIETY, SEPTEMBER 22–25, 1931

HOTEL HADDON HALL, ATLANTIC CITY,

NEW JERSEY

TUESDAY MORNING, SEPTEMBER 22, 1931

Roentgenological and Legal Aspects of the Fractures of the Jaw. S. W. Donaldson, M.D., Ann Arbor, Michigan.

Fractures and Epiphyseal Separation Fractures of the Ankle: A Classification of 325 Cases According to the Mechanism of their Reduction. Paul Bishop, M.D., Philadelphia, Pa.

A Study of the Hip Joint from the Standpoint of the Roentgenologist. L. B. Morrison, M.D., Boston, Mass.

The Evaluation of Ventriculography and Pneumoencephalography. A. W. Adson, M.D., Rochester, Minnesota.

Encephalography in Children. R. Cannon Eley, M.D., and E. C. Vogt, M.D., Boston, Mass.

Explanation of Errors in the Diagnosis of Pituitary Lesions. Henry K. Pancoast, M.D., Philadelphia, Pa.

Sinus Roentgenology. Dorwin L. Palmer, M.D., Portland, Oregon.

Life History of a Lithopedion told by X-ray. L. R. Sante, M.D., and Fred Emmert, M.D., St. Louis, Missouri.

TUESDAY AFTERNOON, SEPTEMBER 22, 1931

Unusual Types of Pneumonia Resulting from Aspiration of Fats and Oils. J. W. Pierson, M.D., Baltimore, Maryland.

Miliary Lung Lesions. R. R. Sayers, A.M., M.D., and F. W. Meriwether, M.D., Washington, D. C.

Varieties of Fuso-Spirochoetal Infection of the Lung. William G. Herrman, M.D., Asbury Park, New Jersey.

Primary Carcinoma of the Lung—Roentgen Ray Diagnosis and Preliminary Report on Roentgen Therapy. Willis F. Manges, M.D., Philadelphia, Pa.

The Therapeutic Application of the Roentgen Ray in Angina Pectoris. E. C. Samuel, M.D., and E.R. Bowie, B.S., M.D., New Orleans, Louisiana.

Status and Clinical Application of Roentgenology of the Thoracic Aorta. John Sproull, M.D., Haverhill, Massachusetts.

TUESDAY EVENING, SEPTEMBER 22, 1931

Caldwell Lecture. Professor Dr. Fedor Haenisch, Hamburg, Germany.

WEDNESDAY MORNING, SEPTEMBER 23, 1931

A Type of Cell Division from its Medical Biology. Stanley P. Reimann, Ph.D. Philadelphia, Pennsylvania.

The Chemistry of Cell Division. F. S. Hammet, M.D., Philadelphia, Pa.

Roentgen Therapy of the Epitheliomas of the Tonsil, Larynx and Hypopharynx, 1920–1926. Henri Coutard, M.D., Paris, France.

Development of Technique and Results in the Treatment of Tumors in the Nasal and Oral Cavities. Elis Berven, M.D., Stockholm, Sweden.

Principles and Methods Employed in the Treatment of Intra-Oral Epidermoid Carcinoma. Douglas Quick, M.B. (Tor.), Attending Surgeon Memorial Hospital, New York City.

WEDNESDAY AFTERNOON, SEPTEMBER 23, 1931

Water Phantom Intensity Measurements of Roentgen Rays Produced by 130,000 Volts. J. L. Weatherwax, M.A., and C. Robb, E.E., Philadelphia, Pennsylvania.

The Principle of Absorption and the Method of Multiple Converging Beams. A. U.

Desjardins, M.D., Rochester, Minnesota.

Radon Seeds Versus Small Radium Needles. Charles L. Martin, E.E., M.D., Dallas, Texas.

Recovery from X-ray Effects as Observed in the Arbacia Egg. P. S. Henshaw, Ph.D., and G. Failla, D.Sc., New York City.

Change in Quality of X-rays at Different Tissue Depths. Edith H. Quimby, M.A., and Robert P. McNattin, M.D., New York, N. Y.

Further Experiences with Gurwitsch's Mitogenetic Radiation. Otto Glasser, Ph.D., Cleveland, Ohio.

Report on the International Comparison of X-ray Standards. Lauriston S. Taylor, Washington, D. C.

A 900,000 Volt X-ray Outfit. W. D. Coolidge, Ph.D., L. E. Dempster, and H. E. Tanis, Jr., Schenectady, New York.

Concerning the Visibility of the Roentgen Ray. Robert B. Taft, B.S., M.D., Charleston, S. C.

THURSDAY MORNING, SEPTEMBER 24, 1931

Roentgen Study of the Vertebral Body. William A. Evans, M.D., Detroit, Mich.

Intrinsic Circulation of the Vertebral Body with Roentgenologic Consideration. G. Wagoner, M.D., and E. Pendergrass, M.D., Philadelphia, Pa.

Further Consideration of Tuberculosis of the Spine. Howard P. Doub, M.D., and Carl E. Badgley, M.D., Detroit, Michigan.

Tuberculosis of the Shaft. R. Bromer, M.D., and E. E. Downs, M.D., Philadelphia.

Benign Giant Cell Tumors. B. R. Kirklin, M.D., and C. M. Moore, M.D., Rochester, Minnesota.

The Treatment of Giant Cell Tumors by Roentgen Therapy. G. E. Pfahler, M.D., Sc.D. and L. D. Parry, M.D., Philadelphia, Pa.

Giant Cell Bone Tumor—A Consideration of the Value of Various Methods of Treatment both Surgical and Radiological. Carleton B. Peirce, M.S., M.D., Ann Arbor, Michigan.

Unfiltered Roentgen Rays for External Cancers of Wide and Deep Involvement. Bernard P. Widmann, M.D., Philadelphia, Pennsylvania.

THURSDAY AFTERNOON, SEPTEMBER 24, 1931

Carcinoma of the Cervix: An Evaluation of the Results of Treatment with 1-Radium Alone 2-Radium Plus Deep Therapy. C. A. Behney, M.D., Philadelphia, Pa.

Treatment of Testicular Malignancies. John T. Murphy, M.D., and T. H. Ramsey, M.D., Toledo, Ohio.

X-ray Therapy for some Tumors of the G.U. Tract. U. V. Portmann, M.D., Cleveland, Ohio.

Experimental Studies of the Blood Following Small Doses of X-ray. Charles A. Waters, M.D., and W. B. Firor, M.D., Baltimore, Maryland.

The Roentgen Management of Lymphoblastoma (Hodgkin's Disease) K. R. McAlpin, M.D., and Ross Golden, M.D., New York City.

Myelogenous Leukemia. Edward L. Jenkinson, M.D., Chicago, Illinois.

Studies of the Diseases of the Lymph Glands from the Hematological and Radiotherapeutic Viewpoint. N. Rosenthal, M.D., W. Harris, M.D., and A. Kean, M.D., New York City.

FRIDAY MORNING, SEPTEMBER 25, 1931

Some Observations in the Use of Intravenous Urography. Karl Kornblum, M.D., Philadelphia, Pennsylvania.

Urography in Urinary Tract Anomalies in Children. Meredith F. Campbell, M.D., New York, N. Y.

Roentgenological Aspect of Pyelitis of Pregnancy. Samuel A. Robins, M.D., Boston, Massachusetts.

An Ascending Foreign Body in the Kidney Pelvis. T. P. Waring, M.D., and R. Drane, M.D., Savannah, Georgia.

Further Investigations in Hepatography and Lienography Following the Administration of Thorotrast. W. H. Stewart,

M.D., M. Einhorn, M.D., and H. E. Illick, M.D., New York City.

X-ray Pelvimetry. A Simplified Stereo-Roentgenographic Method. Paul C. Hodges, M.D., and Alfred C. Ledoux, M.D., Chicago, Illinois.

A Method of Precision Technic for the X-ray Examination of Infants. David R. Bowen, M.D., Philadelphia, Pennsylvania.

Aiding Research in Radiology. Rollin H. Stevens, M.D., Detroit, Michigan.

FRIDAY AFTERNOON, SEPTEMBER 25, 1931

The Roentgen Findings in Progressive Bulbar Palsy. Arthur C. Christie, M. D. From the Radiological Clinic of Drs. Groover, Christie, and Merrit, Washington, D. C.

Pyloric Stenosis with Hypertrophy of the Pyloric Muscle in the Adult. E. P. McNamee, M.D., Cleveland, Ohio.

The Advantages of Fluoroscopic Control in Radiography of the Stomach. G. W. Grier, M.D., Pittsburgh, Pennsylvania.

An Evaluation of Compression Technique in Roentgen Diagnosis of Duodenal Lesions. Milton J. Geyman, M.D., Santa Barbara, California.

Unfamiliar Pathology of the Mucosa and Sub-Mucosa of the Stomach. The Cole Collaborators.

Chronic Oedema of the Mucosa and Sub-Mucosa of the Stomach. W. G. Cole, M.D. New York City.

Diffuse Hyperplasia of the Connective Tissue of the Sub-Mucosa of the Stomach. R. E. Pound, M.D., New York City.

Anatomy of the Lymphoid Follicles of the Mucosa and Sub-Mucosa of the Stomach. R. W. Morse, M.D., New York City.

Pathology of Lymphoid Tissue of the Stomach. L. G. Cole, M.D., New York City.

SPECIAL NOTICE

SPECIAL RAILROAD RATES

ALL members and guests who anticipate attending the Atlantic City meeting in September are requested to purchase one way tickets to the meeting and ask for a convention certificate at that time. If 150 certificates are presented, the return rate on the railroads will be reduced one-half. All members are earnestly requested to ask for these certificates in order that the benefit to the members coming from a distance may be realized on these half fare return tickets.

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, 105 Rutledge Ave., Charleston, S. C.

AN ACCESSORY FOR SERIAL ROENTGENOGRAPHY IN PEPTIC ULCER*

By HOLLIS E. POTTER, M.D.
CHICAGO, ILLINOIS

THE number and variety of devices which have been described during the last fifteen years for the purpose of registering on films the changes seen roentgenoscopically in peptic ulcer emphasize the necessity of some special contrivance for this purpose. The designs produced vary greatly in their complexity and reflect a wide difference in the minds of the designers as to the diagnostic requirements in ulcer. Some consist of a simple film-changing device, while others provide for the rapid serial production of an endless chain of films by mechanism highly specialized in character as in making moving pictures.

Fig. 1. Accessory for serial roentgenography of peptic ulcer. Consists essentially of a padded frame to fit the top of a tilt-table. It houses a film-shifting unit which we call a "quad."

Although the problem of stomach diagnosis has been taken up in a widespread manner by the general roentgenologist, it is noticeable that no manufacturer produces an accessory for this purpose that is recognized as adequate for general use. This again may be explained by the difference of opinion as to the requirements on the part of the users.

The result seems to be that the average laboratory doing general work in a hospital or office is satisfied to produce a haphazard short series of films, made without roentgenoscopic positioning, which to any secondary observer who has not screened the case, cannot rightfully mean much as arguing either for or against an organic lesion. The small laboratory is not justified in maintaining a highly complex apparatus for limited use and the manufacturer wrongfully tries to incorporate a variety of special features in one universal equipment which the agent insists will satisfy every requirement.

If films are to be made at all in connection with stomach and particularly duodenal diagnosis these films must be made at such optimum time and at such optimum angles as have been determined by screen examination. And if they are to be made in

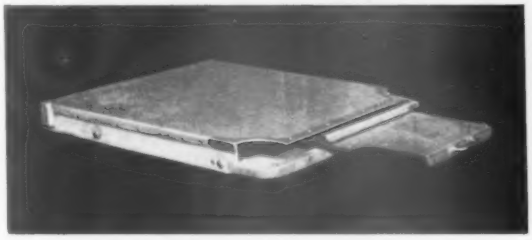

Fig. 2. The "quad" is a separable unit designed only to use in the accessory shown in Figure 1. It allows four 5½″×7″ exposures on each 11″×14″ film. The shift is manual. Four exposures spaced five seconds apart are made during a stomach cycle. When used in high oblique or vertical position the cassette is automatically locked in its "upper" position for the lower pair of exposures.

* This is the sixth of a series of articles on diaphragming roentgen rays.

serial multiples on limited-sized film they must be centered roentgenoscopically. It is not so necessary that the image should be visible on a screen during the exact time of exposure.

Because in duodenal ulcer particularly there is an arrhythmic action of the stomach with periods of active emptying which alternate with periods of quiescence or spasmodic closure of the pylorus, roentgenographic records should be made during the active periods when barium gives good duodenal filling. The roentgenologist should therefore be equipped to turn quickly from a screen observation to a roentgenographic set-up and procure his films at this optimum time.

On account of this same intermittency and perhaps the additional irritability of the duodenal bulb caused by the lesion, haphazard exposures even at this time may miss the period in the stomach cycle when the duodenal bulb is full of barium. Unless full, the confusion between a filling defect

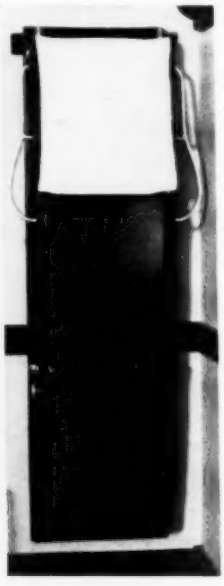

Fig. 3. The frame without the "quad" hangs out of the way on the wall when not in use.

and a simple non-filling may at once arise. It is advisable therefore to make a series of perhaps four exposures during an active stomach cycle in order to catch the bulb full once, twice or more times and to explain the significance of the non-filled periods. The making of such series of four

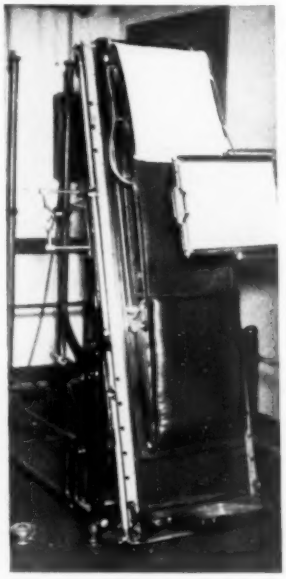

Fig. 4. After preliminary roentgenoscopy the apparatus is transferred to the tilt-table in near-vertical position. Adjustment to the patient's height is made when he first stands to face it. The table is then turned down, the "quad" inserted, and the optimum time and position for roentgenography determined.

during the twenty-second time period for one stomach cycle requires very little extra equipment. If repeated during three, four or five stomach cycles, there will probably result films having true diagnostic import.

During the preliminary screen study the patient will be rotated so as to determine the optimum angle. This is any straight or oblique angle where the pylorus or duodenal bulb is free from overlapping by the antrum and the second portion of the duodenum. At the same time, it is an angle which is found to bring the ulcer crater into profile. Crater ulcers producing no deformity and located anteriorly or posteriorly must be visualized through the bulb after collapse by a rubber bag. At any rate when manipulating the patient for the optimum angle it may be found that a tilting table will aid greatly in avoiding the overlapping effects produced by gravity or in taking ad-

vantage of gravity effects favorable to the particular case.

With these preliminaries in mind one can appreciate the writer's viewpoint and estimate to what extent the apparatus herewith described fulfills the requirements.

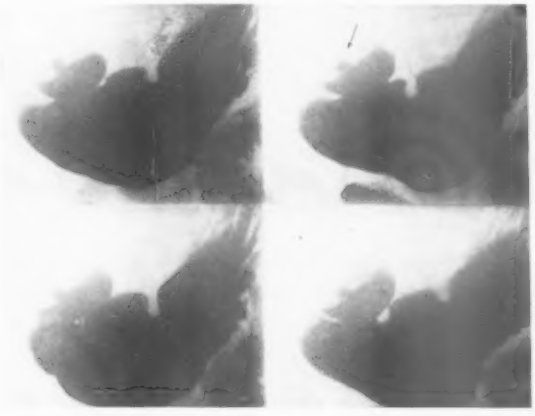

Fig. 5. Showing amount of stomach and duodenum included when using 11"×14" "quad." Here it was possible to place ulcer (arrow) in profile.

The frame is in the form of a false table top designed to hang or lie on top of a stock tilt-table. When not in use it hangs vertically on a nearby wall and it is held vertically when transported to the upright tilt table to be hooked over the top edge. It is more or less shaped to the form of patient's body, is padded above and below with middle exposure section of sheet aluminum unpadded but faced with auto-top material. The patient mounts the footboard of the tilt-table, grasps the hand rail, and the table is tilted back a few degrees to give the patient stability against the frame. In this position the height of the frame is regulated by sliding it up or down on a subframe after roentgenoscopic determination of duodenal height. The table is then turned down to a near-horizontal position and the serial exposure unit inserted in the open chamber beneath the patient's abdomen.

This serial exposure unit which we call a "quad" is leaded on top except for a central quadrangle $5\frac{1}{2}\times7$ inches in size which is merely covered with aluminum. Beneath this opening there are no opaque materials in the quad which prevent roentgenoscopy from the tube below. This opening admits the rays from an overhead tube for roentgenography. Rays pass through it to the quarter of an 11"×14" film held in the cassette which is shifted on a mechanism within the quad after each exposure. For the fine adjustment under the screen of the duodenum or other suspected portion into the center of the $5\frac{1}{2}$"×7" opening the whole quad slides on bearings up and down 4 inches, or slides in or out on its carriage. In the intervals between exposures the film is shifted by hand, thus doing away with all automatic mechanism.

Into the same carriage holding the quad may be inserted three other units occasionally desired in stomach roentgenography. The first is a simple base for spotting and holding a 14"×17" cassette. The second is a simple unit or tunnel for making two exposures on an 11"×14" film, the one half being protected during the exposure of the other.

The third unit is a thin grid diaphragm of flat design built to the size of a 10"×12"

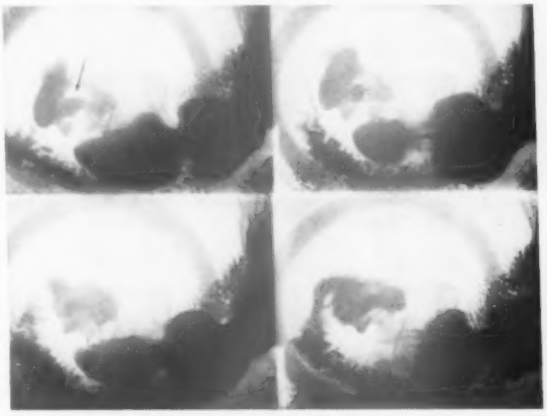

Fig. 6. Full 11"×14" film showing four exposures five seconds apart. Ulcer crater on anterior or posterior wall must be visualized by rubber bag pressure—meniscus sign.

cassette by Buck, or one measuring $11\frac{1}{4}\times13\frac{1}{4}\times\frac{5}{8}$ inches. This diaphragm apparatus is of the same general design as those described in the notes on sinuses and mastoids, only larger. It is so constructed that it may

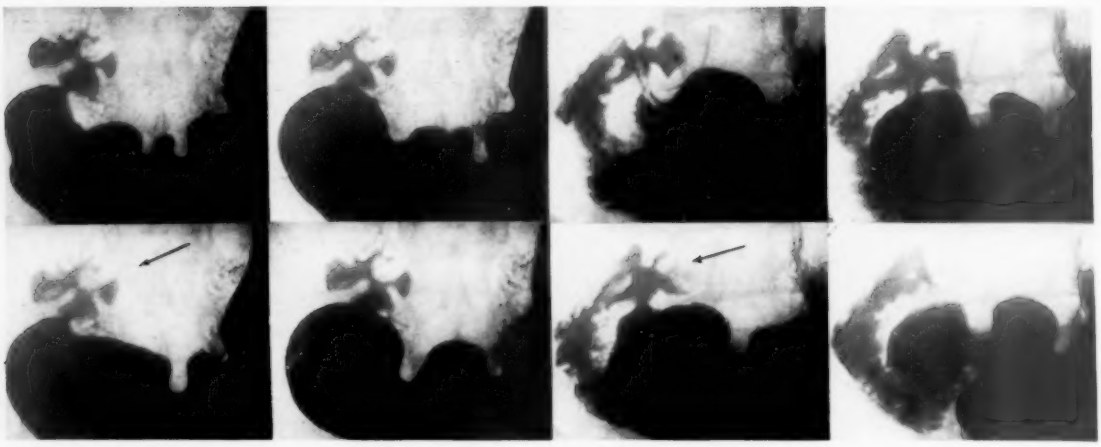

Fig. 7. Two cases where haphazard methods would succeed. The duodenal deformity is pronounced and constant.

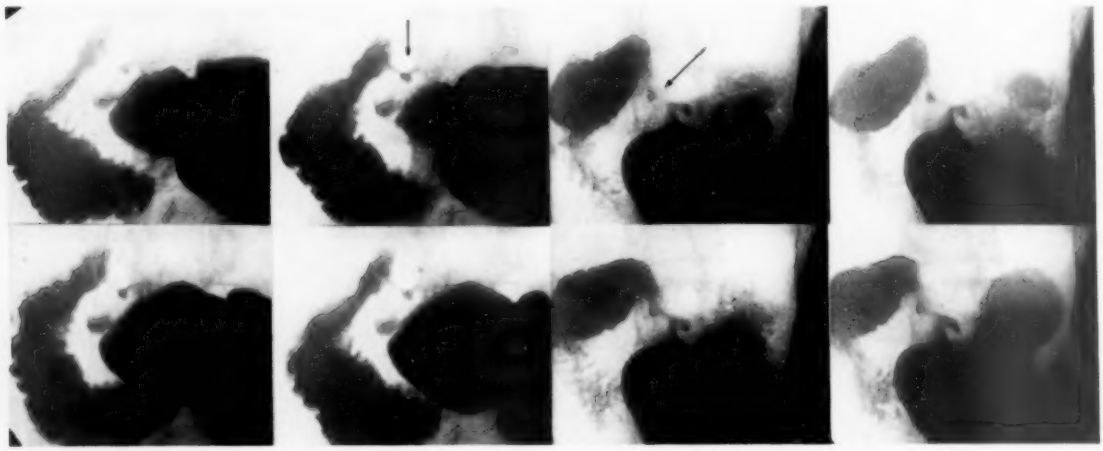

Fig. 8. Two cases of high-grade bulb deformity and crater. The serial method establishes the callous character of the walls.

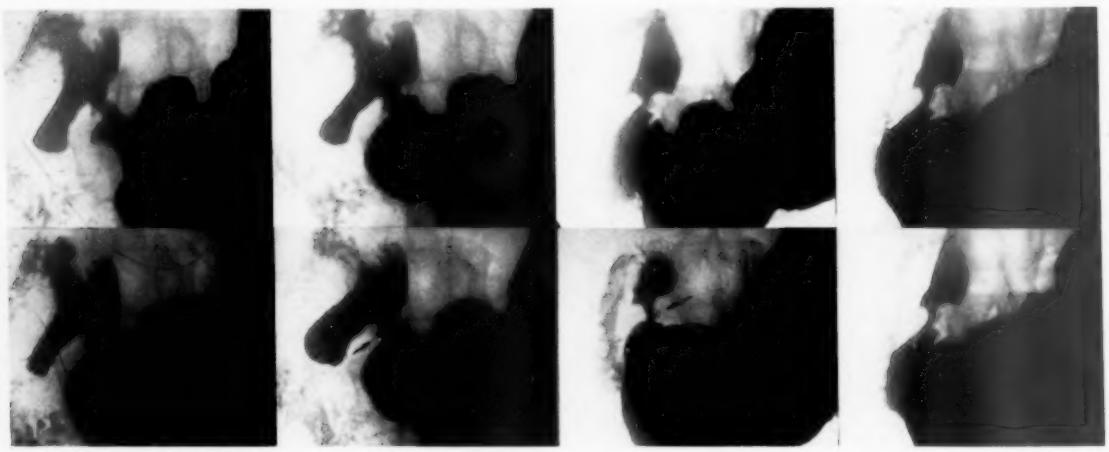

Fig. 9. Two cases of pyloric ulcer showing crater. Here the optimum angle for pylorus and ulcer must be predetermined by roentgenoscopy.

Fig. 10. By previous roentgenoscopic control one can frequently alter factors to show anterior wall craters without bag pressure as in these two cases.

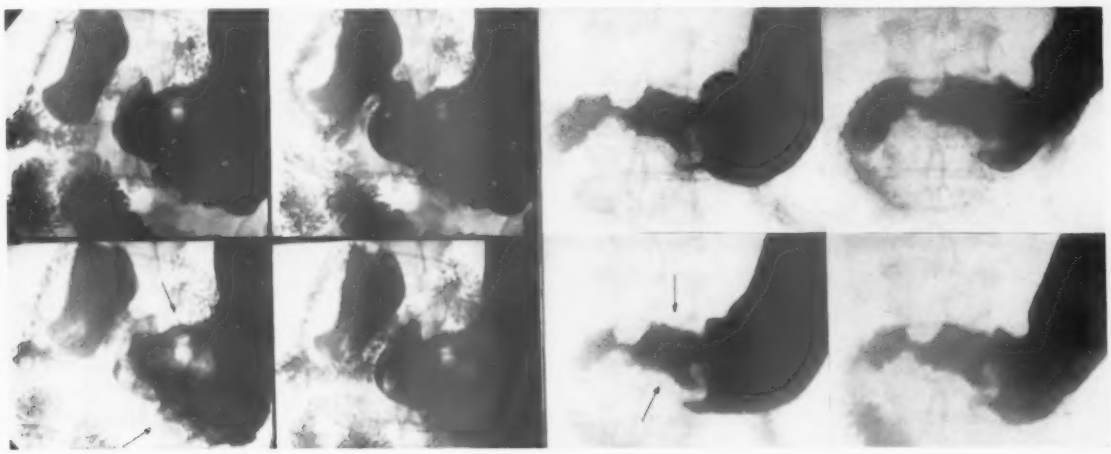

Fig. 11. The filling defects of carcinoma must persist in serial films, while elastic portions of the stomach vary with peristalsis.

Fig. 12. Small ulcer niches on the lesser curvature of the stomach may be wholly lost in films not controlled by roentgenoscopy. Showing two cases.

be used either in conjunction with a special housing on the overhead arc apparatus for comprehensive films of the head, on this stomach unit for stomach or gall-bladder work, or it may be used separately on any other table for any desired purpose. In design it has the advantage again of the greatest economy in patient-film distance, and is no wider than the short side of the 10″ ×12″ cassette. The latter point is of advantage in avoiding shoulder interference in head work whether used on the special stand or on any table.

It may be noted that I do not favor the routine use of the grid diaphragm for localized serial films on the duodenum, considering it neither necessary nor advisable. It is not necessary because a reasonably efficient diaphragming effect may be obtained from the narrowed cone of light used and because the density contrast of the barium meal is so high that the extreme black and white effect produced by the grid is of no advantage. It is not advisable because rapidity of exposure is often the essence of success and because the increased patient-film distance robs the definition of barium outlines without adequate compensation. In the exceptional case, however, the grid is of advantage, particularly in obtaining comprehensive views of the stomach and bowel.

If one's technique in rapid serial duodenal roentgenography demands the grid diaphragm for contrast a grid of the spiral form, thin, of low ratio and incorporated in a film-shifting device similar to the quad would be recommended. Because of the continuous movement of the spiral the grid would not have to be tended and the number of operations during exposure not increased. I have designed such a unit but have seen no reason to have it built.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Vallebona, A. Una modalita di tecnica per la dissociazione radiografica delle ombre applicata allo studio del cranio. (A technical method for roentgen dissociation of the shadow applied to the study of the skull.) *Radiol. med.*, Sept., 1930, *17*, 1090–1097.

Ordinarily the shadows of the different bones of the skull are superimposed on each other and make it very difficult to read the roentgenogram. The author describes a method of dissociating these superimposed shadows and getting the shadow of only the part that is wanted. While the roentgenogram is being taken the head is made to undergo a slight rotation by means of an apparatus constructed especially for this purpose. This rotation is on the axis of the region to be examined. In this way the region on the axis of rotation is brought out very clearly on the roentgenogram dissociated from all other shadows. But still another measure is necessary to make the pictures very distinct, especially if the region to be examined is at a distance from the plate. The anticathode focus is never a point and in tubes of high intensity it is quite a large surface; this results in the picture at a distance from the plate never being very distinct. Therefore a tube with a very small focus should be used or else that method should be used which the author described in 1928 under the name of micro-radiography. By this latter method it is possible not only to get enlargements but to take more detailed pictures.—*Audrey G. Morgan.*

Balestra, Giovanni. Sulle calcificazioni della falce cerebrale. (Calcifications of the falx cerebri.) *Arch. di radiol.*, 1930, *6*, 731–747.

The author describes two cases, in one of which roentgen examination showed a large isolated calcification of the falx and the other multiple granular calcifications. He thinks it possible in some cases to differentiate by roentgen examination between osteomas and granular calcification. As to their pathological significance, he believes that while some calcifications and osteomas in particular are mere chance findings, in other cases they are manifestations of a meningeal reaction, from different processes which may be at a distance. Granular calcifications, particularly if not limited to the falx alone, are more apt to be manifestations of pathological changes than osteomas.

In his first case the patient came for treatment for severe headache. He had a positive Wassermann and the headache stopped on specific treatment. In the other case the patient came for examination for a head trauma. The calcifications had not caused any symptoms.—*Audrey G. Morgan.*

Ratti, A. Ricerche di tecnica, di anatomia e di semeiotica radiografiche della rocca petrosa. (Roentgen study of the technique of examination, anatomy and symptomatology of the petrous bone.) *Radiol. med.*, Aug., 1930, *17*, 916–932.

The author describes and illustrates his method of taking pictures of the petrous portion of the temporal bone. The pathological processes found are fractures, inflammations and tumors, the latter being the most common. Tumors may be so large as to destroy the whole of the bone to the median side of the labyrinth. The complex structure of the bone makes a special technique necessary. The projections generally used are the transorbital, the axial, Stenvers' projection and the fronto-suboccipital.

The parts of the bone that require examination are the apex, the porus and internal auditory meatus and the upper margin. The apex may show erosions of the bone caused by tumors. The two sides should be compared in order not to confuse a destructive process in the lower half with the convexity upward with the picture of the carotid canal. An enlargement of the porus acusticus internus may be the only sign of tumor of the auditory nerve. It is hard to demonstrate, however, for the porus on the two sides may be of different sizes normally. The size of the picture of the porus is also influenced by the degree of flexion of the head. The auditory meatus is also dilated when the porus is dilated. Erosions of the upper margin may be caused by tumors also. But just to the median side of the arcuate eminence there is often a

small incisure of a depth of about a millimeter. It corresponds to the projection of the upper end of the subarcuate fossa and the adjacent tract of the superior petrosal sinus and should not be confused with a pathological lesion.

The author made roentgenograms of the petrous bone in cadavers after having made experimental lesions, in order to study the characteristic pictures. He thinks a systematic examination of the petrous bone should include examinations in the two sagittal and axial projections and in Stenvers' projection for details of the lower surface.—*Audrey G. Morgan.*

Santoro, Mario. La pneumo-ventriculografia in due casi di affezioni cerebrali. (Pneumoventriculography in two cases of brain disease.) *Radiol. med.*, Sept., 1930, *17*, 1054–1062.

Two cases of brain disease are described in which pneumoventriculography was practised and the ventriculograms are given. The first case was one of essential internal hydrocephalus. In the second a large subdural hematoma was exercising pressure on the right cerebral hemisphere. The author was struck in the first case by the diagnostic value of the method which proved perfectly harmless, as shown by the fact that the patient was able to undergo a surgical operation a few days later. He thinks that the method may even be useful in treatment in essential hydrocephalus. There was improvement in his case and other cases have been reported in which there was improvement in the symptoms after ventriculography. These cases, like others previously published, show the diagnostic value of the method, particularly in beginning cases of internal hydrocephalus and in brain tumors, the localization of which is doubtful. But it is a method that requires great care and is not altogether free from danger and is to be used only in cases in which it is strictly indicated.

His second case shows, contrary to the opinion of Schmorl, Rost and Dandy, that the lateral ventricles can be insufflated by Bingel's lumbar puncture, the gas passing through the foramina of Luschka and Magendie.—*Audrey G. Morgan.*

Worms, G., and Didiée, J. Sur un cas de pneumatocèle intra-cranienne post-traumatique de la région frontale: aspects radiographiques. (On a case of intracranial, post-traumatic pneumatocele of the frontal region; roentgen aspects.) *Bull. et mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 408–414.

The authors describe and discuss in lengthy detail a case of pneumatocele of the frontal region which occurred in a jockey twenty-five years of age who fell off his horse and fractured the anterior fossa of the base of the skull. A roentgenogram eight days following the injury revealed no abnormality except a fracture line. A second roentgenogram forty days later showed an air pocket the size of an orange in the right frontal region. This persisted at a third examination ten weeks later but had disappeared at a fourth examination four months later. The case resulted in complete healing.—*T. Leucutia.*

Payenneville, J., and Cailliau, F. Acromégalie avec syndrome adiposo-génital et glycosurie d'origine syphilitique. (Acromegaly with adiposo-genital syndrome and glycosuria of syphilitic origin.) *Presse méd.*, Mar. 14, 1931, *39*, 380–384.

The authors describe in lengthy detail a case of pituitary disturbance which was the result of tertiary syphilis. The case report is briefly as follows: A girl, born at term, and showing normal development, contracted syphilis at the age of twenty. Nine injections of salvarsan were given; then further treatment was refused. At the age of twenty-three the menstruation ceased and at the age of twenty-four, she became very obese, developing at the same time signs of acromegaly. At the age of twenty-eight, the first symptoms of diabetes appeared. The patient was examined by the authors in October, 1929, at the age of thirty-five. Shortly afterward, she went of her own accord to another hospital where she died in December, 1929.

In résumé, the findings were those of a tertiary syphilis (associated with alcoholism and cardiopathy) leading to involvement of the pituitary gland and resulting in several clinical syndromes, such as adiposo-genital syndrome, cranial hypertension, compression of the cavernous sinus with ocular paralysis and strabismus and glycosuric syndrome.

The authors made very minute studies of the changes of various portions of the pituitary gland and found that their case, in certain respects, confirmed the neurocrine (instead of endocrine) conception of Collin with regard to

the histophysiologic function of the pituitary gland. It seems that the sympathetic system through its connection with the histiocytic system plays an important rôle in the circulation of the hormone and its chemical transformation.— *T. Leucutia.*

Santoro, Mario. Disostosi lacunare ipofisaria. (Lacunar hypophyseal dysostoses.) *Arch. di radiol.*, 1930, *6*, 713–730.

A boy of eleven had diabetes insipidus which began suddenly. He was sent for roentgen examination of the sella turcica, which was found normal. On the left parietal bone there was an area about the size of a quarter which was painful on pressure and the mastoids were painful on pressure. The child had slight cervical scoliosis with the convexity to the left and moderate rotation of the head which could be overcome passively, but with great pain. Pressure on the spinous processes of the cervical and lumbar vertebrae the spines of the ilium, the crests of the ilium and the sciatic processes was very painful. Roentgen examination showed rarefaction at the place on the parietal bone that was sensitive to pressure. There were similar rarefactions in the ribs, bones of the pelvis, left humerus and both femurs. Taken in association with the clinical findings, these lesions of the bones were attributed to a lesion of the hypophysis or other nerve centers having to do with calcium metabolism. As the child had pulmonary tuberculosis, fever and cough, it seemed probable that tuberculosis of the above-mentioned centers had caused the bone lesions.— *Audrey G. Morgan.*

Goodyear, Henry M. Use of iodized oil in diagnosis of nasal sinus conditions. *J. Am. M. Ass.*, Oct. 4, 1930, *95*, 1002–1007.

Visualization of the antra by iodized oil is of great value and should be an almost routine procedure in cases of suspected sinus disease. Maxillary sinus disease, contrary to the usual belief, is usually primary and disease of the other sinuses is probably secondary as a rule. Change of position readily causes the opaque fluid to flow from the antra to the ethmoid and frontal sinuses and it is assumed that pus acts in a similar manner. The technique of the injection method is explained. The dangers of preliminary irrigation in causing mucosal swelling and leading to false diagnosis are considered. The authors have noted a beneficial effect following repeated injections of iodized oil, especially in atrophic rhinitis.—*E. W. Hall.*

Granger, Amedee. Roentgen examination of the paranasal sinuses and mastoids. *J. Am. M. Ass.*, Nov. 1, 1930, *95*, 1332–1335.

The Granger position described in 1923 is still the method of choice in the study of the sphenoids and posterior ethmoids. The Granger line is of great value in diagnosis. An experienced roentgenologist can make the necessary diagnosis in the vast majority of cases without the use of iodized oil.

The Granger position for study of the mastoids is superior in that it gives a more detailed view of the mastoid region with fewer structures superimposed. The Law position is the only satisfactory one for children under six years of age. The visualization of the anterior sinus wall in children under two years of age is indicative of a destructive process, except where the mastoid is unusually well pneumatized. Irradiation incident to making of roentgenograms was followed in many cases by resolution and cure. Destruction as revealed by roentgenogram and operation is often much greater than clinical findings would indicate.— *E. W. Hall.*

Parenti, Silvio. La radiologia dentaria nelle sue più comuni applicazioni. (The most common applications of dental radiology.) *Radiol. med.*, Aug., 1930, *17*, 940–967.

The author describes the roentgen anatomy of the teeth according to the views of the modern German school of odontology, which considers the tooth and the neighboring structures —the gum properly speaking, the periodontium and the alveolus as a single dental organ. He describes in detail the technique of intraoral roentgenography and the methods recently introduced by Winter and Raper, and discusses the important contributions which dental roentgenology has made to the diagnosis and treatment of caries and the different forms of periodontitis with their complications, paradentitis and paradentosis.—*Audrey G. Morgan.*

NECK AND CHEST

Kahlstorf, A. Beitrag zur Röntgendiagnose seltener bösartiger Gewächse der Speiseröhre. (Contribution to the roentgen diagnosis of rare malignant growths of the esoph-

agus.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1930, *42*, 421–435.

The authors describe in detail two cases of rare neoplasms of the esophagus. In the first, there was a carcinosarcoma with extensive metastases of the sarcoma components to nearly all organs of the body, chiefly to the subperiosteal portions of several of the bones. In the second, the condition was a carcinoma sarcomatodes with metastases to the paratracheal and cervical lymph nodes and to the liver.

In connection with these two cases, the author reviewed the entire literature and was able to collect 13 cases in the period from 1902 to the present date. These cases are presented in tabular form.

A differential diagnosis from other malignant or benign neoplasms purely on the roentgen appearance is impossible.—*T. Leucutia.*

Feci, L., and Pietrantoni, L. Di alcuni reperti radiografici nella tubercolosi laringea. (Roentgen findings in tuberculosis of the larynx.) *Radiol. med.*, Aug., 1930, *17*, 987–1005.

The author studied three groups of cases—normal subjects, those with other forms of tuberculosis without clinically demonstrable signs of tuberculosis of the larynx and those with recent and old tuberculosis of the larynx. The findings are described and illustrated with roentgenograms and histological photographs. He found that direct observation of the larynx in the latero-lateral projection, the same as used for study of the spinal column, gives a very clear picture of the larynx. In subjects with tuberculosis elsewhere than in the larynx, examination showed precocious ossification, which however followed the lines of development of normal ossification; or in some cases there were scattered zones of calcification, particularly in the posterior segment of the larnyx. These changes might even have been the results of a former slight tuberculosis of the larynx that had not been manifest clinically. In general, it may be siad that in tuberculosis of the larynx there are two histological stages: one of necrosis and a later one of reparative ossification and calcification and that the roentgen picture of the first of these shows rarefaction and of the second condensation. But it is hard to demonstrate the former at a stage when it cannot yet be demonstrated by laryngoscopic examination and the latter does not differ greatly from the picture of other forms of chondritis and perichondritis. The author concludes therefore that roentgen examination is of only relative value in tuberculosis of the larynx and secondary in importance to laryngoscopic examination.—*Audrey G. Morgan.*

Pancoast, Henry K. Roentgenology of the upper respiratory tract. *J. Am. M. Ass.*, Nov. 1, 1930, *95*, 1318–1321.

The study of the soft tissues of the neck has long been neglected, very little practical work having followed the physiologic roentgen studies made in the years from 1909 to 1914. The function of the structures of the pharynx and larynx must be observed fluoroscopically as well as studied by films. The normal swallowing act is described as well as the normal larynx. A few fundamental pathologic conditions are briefly summarized. Phonation is also described and observations made on a speech mechanism following laryngectomy are reported.—*E. W. Hall.*

Jackson, Chevalier L. The diagnosis of laryngeal disease. *J. Am. M. Ass.*, Nov. 1, 1930, *95*, 1322–1325.

Thirteen typical cases of patients with difficulty in swallowing, hoarseness or pain are reported. Patients presenting a chief complaint of hoarseness should have a complete history, mirror laryngoscopy, roentgenologic study of neck, chest and usually of sinuses, complete physical examination, blood Wassermann, sputum analysis and perhaps direct laryngoscopy and biopsy. Roentgenologists can now detect incipient neoplastic and inflammatory lesions of the larynx. Roentgen study by both fluoroscopic and film methods is indicated.—*E. W. Hall.*

Lynch, Kenneth M., and Smith, W. Atmar. Asbestosis bodies in sputum and lung. *J. Am. M. Ass.*, Aug. 30, 1930, *95*, 659–661.

Asbestosis has recently been recognized as a cause of occupational lung disease, the condition having been assumed to be one of silicosis. Asbestosis bodies consist of crystals of asbetos upon which are deposited nodules and segments of a highly refractive substance containing iron. They may be found at autopsy in the lung tissue but examination of the sputum of asbestos workers frequently reveals them. The manner of formation, the time of exposure needed to produce them as well as the exact

chemical nature of the deposits on the crystal await further study.—*E. W. Hall.*

Cole, L. G., Morse, R. W., Pound, R. E., Headland, C. I., and Cole, W. G. The site of predilection in cross-infection from the right to the left lung. *Radiology*, Dec., 1930, *15*, 627–636.

Infections of the right lung which result in destruction of pulmonary tissue not infrequently give rise to infection in the opposite lung. This is termed "cross-infection" by the authors. They consider it an autogenous infection due apparently to the inhalation of infectious exudate and detritus. Although cross-infection of this type may occur in any part of the left lung, there is such a tendency for it to occur in a region midway between the apex and base that this can be considered the site of predilection. In roentgenograms made in the usual posteroanterior projection this area lies between the second and fifth ribs. The entire area may be involved but usually the focus, if early, will be limited. When a destructive lesion involves particularly the right upper lobe one would expect aspiration infection of the right lower lobe to precede cross-infection, for the bronchus to the right lower lobe is an almost direct continuation of the trachea. This type of secondary infection does occur, usually in association with cross-infection, but is most often limited to the peribronchial tissues. In certain cases, however, secondary infection of the lower lobe is more extensive than the cross-infection. The authors present numerous roentgenograms illustrative of cross-infection in tuberculosis and bronchopneumonia.—*J. D. Camp.*

Walther, H. E. Die Röntgenuntersuchung der Stellungspflichtigen und Rekurten in der schweizerischen Armee. (Roentgen examination of conscripts and recruits in the Swiss army.) *Acta radiol.*, Sept. 30, 1930, *11*, 411–424.

The author describes his experience in the Swiss army in the roentgen examination of the lungs of recruits. Screen examination of 20,000 men during the years 1927 to 1929 showed that 1 per cent of the conscripts had symptoms of chronic tuberculosis of the lungs of which they knew nothing themselves. Such symptoms were found in from 4 to 5 in a thousand even among recruits who had already passed through several medical "filters." The roentgen pictures showed chiefly indurative changes, in half the cases involving both upper lobes.

The after-control maintained with regard to these cases of lung tuberculosis which were taken over by the Swiss Military Insurance shows that the recruit-schools where a thorough roentgen examination of the material was made, contributed three or four times less tuberculosis cases than the others. The infantry recruit schools in the divisions where roentgenoscopic examination of the conscripts was made showed many less cases of tuberculosis than the others. The three divisions where screen examination is made with 22 schools contributed 1 case of tuberculosis (1:22) while the others with 32 schools contributed 15 cases (1:2).—*Audrey G. Morgan.*

Bergerhoff, W. Interstitielle Lungenlues. (Interstitial pulmonary lues.) *Fortschr. a. d. Geb. d. Rontgenstrahlen*, Oct., 1930, *42*, 478–485.

Interstitial pneumonic infiltrations in lues start, as a rule, from the hilus and spread along the lymph vessels to the peribronchial, perivascular and interlobar connective tissues. This results in a marked increase of density of the hilar shadow with striations to the middle and lower lobes, the right lower lobe being chiefly involved. Occasionally rounded or irregular shadows appear also within the lung parenchyma. The condition as a whole is not unlike that of cardiac stasis from which a differential diagnosis is often impossible.

Three cases in which antiluetic treatment led to complete disappearance of the changes within the chest are briefly described and illustrated with roentgenograms taken before and after the treatment. In a fourth case, which is also briefly mentioned, the diagnosis has remained somewhat obscure.

It is the author's contention that luetic pulmonary changes occur more often than hitherto supposed. Roentgen films of the chest are of great diagnostic aid in such instances.—*T. Leucutia.*

Rivers, T. M., Benjamin, Bernard, and Berry, G. P. Psittacosis. *J. Am. M. Ass.*, Aug. 23, 1930, *95*, 577–579.

The case of a physician who contracted the disease during experimental work is reported. The symptoms and course are described in detail along with the laboratory findings. It is emphasized that while physical signs and roent-

genographic studies revealed the presence of pneumonia there were practically no symptoms of respiratory tract involvement. The pneumonic process, unilateral and central in type, was observed roentgenographically to vary markedly, with periods of progression and regression. It simulated influenzal pneumonia rather than bronchopneumonia.—*E. W. Hall.*

Rivers, T. M., Berry, G. P., and Rhoads, C. P. Psittacosis; observations concerning the experimental disease in parrots, mice, rabbits, guinea-pigs and monkeys. *J. Am. M. Ass.*, Aug. 23, 1930, *95*, 579–583.

Experimental studies with parrots, rabbits, mice and monkeys show the usual point of entry of the infectious agent to be the mucous membrane of the upper respiratory tract. As would be expected the pathologic changes in monkeys most closely simulate those observed in man, the chief lesion being a hilar pneumonia. Small "bacteria-like" bodies found in some cases are not shown to have a definite connection with the disease.—*E. W. Hall.*

Jackson, Chevalier. The mechanism of physical signs in neoplastic and other diseases of the lung; with especial reference to atelectasis and emphysema. *J. Am. M. Ass.*, Aug. 30, 1930, *95*, 639–644.

A thorough understanding of the mechanism of the production of physical signs in lung diseases is of vital importance to their proper interpretation. Neoplasms, granulations, swellings and dried secretions, and endogenous foreign bodies, produce signs similar to exogenous bodies. Bronchial obstruction is of the type represented mechanically by the stop valve, check valve, and by-pass valve. Bronchoscopy can determine which type is present and is especially important in diagnosis of check valve lesions and removing a frequent cause of atelectasis.—*E. W. Hall.*

Drevon. Kyste hydatique du poumon. (Hydatid cyst of the lung.) *Bull. et mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 478.

This is a very brief case report of a hydatid cyst of the lung which was verified at operation. The case is described on account of the fact that it exhibited sharp borders on the roentgenogram without producing any reaction of the surrounding tissues.—*T. Leucutia.*

Huguet, Emperaire and Zucoli. Un cas de kyste hématique pleural calcifié. (A case of calcified hematic cyst of the pleura.) *Bull. et mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 464–467.

A case of an interesting calcification occurring in a hematic cyst in a man fifty-one years of age is described and illustrated with two roentgenograms. The only symptoms were occasional pain in the right hemithorax lasting for a period of about a year and a sensation of the presence of a rigid intrathoracic foreign body.—*T. Leucutia.*

Silveira, José. Doit-on considérer comme pathologique l'aorte descendante lorsqu'elle est visible aux rayons X? (Should one consider as pathologic the descending aorta visible to the roentgen rays?) *Presse méd.*, Feb. 21, 1931, *39*, 268–271.

The author describes in detail his technique for the roentgen visualization of the descending aorta, which is as follows: The patient is placed with the back against the screen or film and the tube is moved to the right and angulated so that the central ray enters the thorax anteriorly on the right side and emerges posteriorly on the left side, thus taking a direction similar to that in the left posterior oblique position. This new projection is somewhat similar to the "eccentric roentgen projection" of Groedel, and is called by the author "right anterior extra-central projection." Depending on the degree of the inclination of the tube, it will lead to various roentgen appearances of the descending aorta. Thus if the inclination is from 10 to 20°, the descending aorta will form a part of the heart shadow appearing in the form of a dense opacity from the tracheal bifurcation to the diaphragm. If the inclination is from 30 to 45° it will appear in the form of a shadow of double density, darker towards the heart and lighter towards the right, the vertebral portion being separated from the spinal column by a small transparent zone, the so-called "vertebro-aortic space." If the inclination is about 50° the descending aorta will appear the clearest, its entire shadow being of a uniform density.

In estimating the intensity of the roentgen shadow of the descending aorta one will proceed in practice as follows: (*a*) a preliminary roentgenoscopic examination is made in the routine right anterior and right posterior oblique positions, and if the aorta appears as "if

injected by barium salt," a diagnosis of abnormal opacity of the aorta is made; (*b*) if the descending aorta cannot be visualized clearly enough in the classic positions, roentgenograms are taken according to the author's technique by using various inclinations of the tube. It must be mentioned, however, that one must be extremely careful in the interpretation of the intensity of the shadow.

The conclusion is reached that the visualization of the descending aorta on the screen or film does not indicate a pathologic condition. A true estimation of the density of its shadow can be obtained only after most minute study and with perfect technique.—*T. Leucutia.*

Podkaminski. Existe-t-il une hypertrophie du coeur causée par le travail? (Does there exist a hypertrophy of the heart caused by work?) *Bull. et mém. Soc. de radiol. méd. de France*, Nov., 1930, *18*, 373–374.

The author made a prolonged study (from 1920 to 1930) on the effect of overwork on the heart, by using teleroentgenography at 2 meter distance. The subjects examined were divided into two groups: (1) those performing very heavy labor (longshoremen carrying on their backs 25 tons a day), and (2) those performing sedentary work (seamstresses). The series included 450 men and 600 women.

The subjects were classified according to their weight and height, and the relation of the horizontal diameter of the heart to both weight and height was determined. It was found that this relation was smaller for the longshoremen and larger for the seamstresses. The systolic pressure was decreased in the longshoremen (106 mm.) and increased in the seamstresses (115 mm.), while the pulse was more rapid in the former (114) and slower in the latter (83).

According to the author, the relative small size of the heart and the acceleration of its rhythm in the heavy workers is due to three causes: (1) diminution of the capacity of the heart; (2) compression of the cardiac muscle, and (3) hypertrophy of the heart due to sympathetic action. The relative increase in the size of the heart of seamstresses must be attributed to the sitting position leading to a portal hypertension and capillary stasis.

The conclusion is reached (1) that the professional occupations influence the dimensions of the heart to an appreciable extent and (2) that a hypertrophy of the heart due to physical labor does not exist.—*T. Leucutia.*

Nebout, J. Orthoradiographie du coeur. (Orthoroentgenography of the heart.) *Bull. et mém. Soc. de radiol. méd. de France*, Nov., 1930, *18*, 363–367.

The author describes a simple method for the roentgenography of the heart associated with orthodiagraphy which he calls polyorthoroentgenography of the heart. It consists in the preliminary orthodiagraphic localization of the four points G, G', D and D' of the heart, and the taking of four roentgenograms on the same film with the central ray directed over each of the points.

The following is the practica lprocedure: The patient is placed behind a roentgenoscopic screen and immobilized. Point G' is localized by roentgenoscopy and the normal ray centered over it The diaphragm is then slightly opened and the first roentgen exposure of the heart made. After removal ot the cassette point G' is localized in a similar manner and a second exposure made with the normal ray centered over it. The procedure is then repeated for points D and D'.

All points of the heart having in the roentgenogram a normal orthodiagraphic relation, the diameters can be easily determined. They will have the precise orthodiagraphic values.

The advantages of the method are that it can be used both in the vertical and horizontal positions and that the borders of the heart appear more clearly than in teleroentgenography. The disadvantages are that the procedure is rather cumbersome, that a good immobilization is necessary and that the various exposures must be made with the same respiratory immobility. In this latter respect it is best to use short exposures at the end of expiration and during diastole.—*T. Leucutia.*

ABDOMEN

Belot, J., Gally and Dhikéos. Contribution à l'étude radiologique des estomacs biloculaires. (Contribution to the roentgen study of bilocular stomachs.) *J. de radiol. et d'électrol.*, Dec., 1930, *14*, 625–633.

The authors made a detailed study of bilocular stomachs from the standpoint of their roentgen appearance. The following classification is used: (1) Pseudo-biloculation of the stomach. (*a*) Cascade stomach. This is due to a most probably congenital anatomic predisposition of the stomach, consisting in a posterior subdiaphragmatic displacement of the great tuberosity and

a shortening and narrowing of the corpus. Roentgenologically two pouches are distinguished communicating with each other in the form of a "cascade." It is the authors' contention that this type always represents a false biloculation, the pouches disappearing easily as a result of manipulation or during the change of position of the stomach. Other investigators have called attention to the fact that there is often a localized perigastritis producing adherence of the posterior wall of the stomach to the diaphragmatic dome, but the authors were unable to find inflammatory changes in any of their cases examined. (*b*) Biloculation by compression or pull. Of the neighboring organs, especially the spleen, left lobe of the liver and left colon are those which may give rise to conditions causing compression of the stomach (cancer, benign tumors, cysts, inflammatory conditions, etc.). The biloculations due to compression are characterized chiefly by instability, variation of the compression in time and space, and conformation of the defect to the size and shape of the pressing lesion. The authors observed one single case of biloculation due to pull on the stomach. Here there is an extremely elongated stomach with pull of the barium-filled lower pole on the weakened longitudinal fibers. Taken as a whole, the biloculation by pull is the inverse picture of the cascade stomach.

(2) True biloculation of the stomach. This type of biloculation is characterized by constancy in space and in different positions although there may be a variation in time. One of its chief diagnostic signs is that it persists on palpation. Two forms are distinguished: (*a*) B-form. Here the lesser curvature of the stomach is rather straight, maintaining a normal outline, while the greater curvature presents a contraction, chiefly of spastic origin, which divides the stomach into two symmetrical parts. The condition is encountered in ulcer of the lesser curvature and less frequently in inflammatory reactions of the abdominal viscera (cholecystitis, appendicitis, etc.). The administration of antispasmodics (papaverin, atropin) or anesthetics (ethyl chloride, amyl nitrate, ether or chloroform) occasionally relieves the spasm leading to disappearance of the biloculation. It must be mentioned, however, that a persistence of the spasm in spite of the administration of the above drugs does not necessarily indicate an organic lesion. (*b*) Hourglass form. This condition is always the result of an organic lesion. Constancy in time and space form its chief characteristics.

(3) Rare types of biloculation: (*a*) Postoperative biloculation This is sometimes found following insufficient resection of a large sclerosed zone of the stomach. It represents a functional disturbance and as a rule disappears with the return of the normal motor function of the stomach. (*b*) Biloculation due to foreign bodies (needle, safety pin) or to caustic liquids which have irritated the lesser curvature of the stomach, as a rule of only temporary duration. (*c*) Biloculation due to rhinitis plastica, characterized by a progressive narrowing of the body of the stomach. (*d*) Biloculation produced by diaphragmatic hernia, the upper part of the stomach having entered the thoracic cavity.

The article is illustrated with some unusual, beautiful roentgenograms.—*T. Leucutia.*

Anzilotti, A. Sulle immagini diverticloari dello stomaco. (Pictures of diverticula of the stomach.) *Radiol. med.*, Sept., 1930, *17*, 1033–1048.

The author describes and illustrates a case of diverticulum of the stomach and reviews what has been written on the subject from the point of view of both roentgenology and pathology. He does not recognize the so-called "functional diverticula" that are described by some authors, but thinks that they are caused by mistaken interpretations of roentgen pictures. On this point he cites De Quervain who at first believed in these functional diverticula and then changed his opinion.

He describes the classical symptoms in roentgen diagnosis of diverticulum: the picture of persistent paragastric diverticulum with an air bubble, a neck connecting it with the stomach, its characteristic site and peristaltic function and its displacement with the stomach shadow on any change in position of the patient's body. The "peninsula appearance" as the author calls it, is quite characteristic. Differential diagnosis must be made from perforating ulcer and from diverticula of other parts of the intestinal tract. In the latter the diverticula do not move with the stomach shadow. He thinks that certain spastic phenomena described by Brdiczka under the name of "antral pseudo-diverticula" are not diverticula.

His case was one of diverticulum of the greater curvature from adhesive perigastritis, similar to another case which he saw a few years before.—*Audrey G. Morgan.*

Klason, T. On great gastric retention and dilatation of the stomach in cases of gastroduodenal ulcer and cancer of the stomach. *Acta radiol.*, Sept. 30, 1930, *11*, 444–450.

The author made a study of the frequency of great retention and dilatation of the stomach in cases of gastroduodenal ulcer and cancer of the stomach. Among 451 cases of ulcer this complication was present in 39 cases, or 8.6 per cent. Among these ulcers 258 were duodenal, and among these there was great gastric retention in 28, or 11 per cent. There were 193 gastric ulcers and this complication occurred in 11 cases, or 5.7 per cent. Among 201 cases of cancer of the stomach there was total or subtotal infiltration of the whole stomach in 19 cases, or 9.4 per cent; the tumor was in the canal in 97 cases, or 48 per cent, and in the fornix, body or sinus in 85 cases, or 42 per cent. Great retention and dilatation of the stomach were found only in cases of cancer of the canal, being present in 30 cases out of 97, or 31 per cent, and in 14.3 per cent of all cases of cancer of the stomach. —*Audrey G. Morgan.*

Guénaux, G., and Vasselle, P. Les méthodes d'imprégnation de la muqueuse intestinale. (Impregnation methods of the intestinal mucosa.) *Bull. et mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 404–408.

The authors employed umbrathor by following Kalkbrenner's procedure (250 c. c. umbrathor in 600 c.c. water in the form of an enema) for the roentgen visualization of the mucous membrane of the colon.

The method is of value in the differentiation of the various forms of colitis (ulcerous colitis, dysentery, tuberculosis, etc.), and in the early diagnosis of neoplastic lesions.—*T. Leucutia.*

Fleurant. Un cas d'interposition hépato-diaphragmatique par les anses grêles. (A case of hepato-diaphragmatic interposition of the small intestinal loops.) *J. de radiol. et d'électrol.*, Dec., 1930, *14*, 640.

This is a very brief case report of a man fifty years of age who came to roentgen examination with a clinical diagnosis of pyloric ulcer. At the six and twenty-four examination following the administration of a barium meal it was found that certain loops of the small intestine were lodged between the liver and diaphragm giving a very unusual appearance. Unfortunately the case could not be verified operatively since the patient had refused surgical intervention.—*T. Leucutia.*

St. Simon. Zur Kenntnis des Verhaltens des Wurmfortsatzes und des Blinddarmes bei Schwangeren. (On the knowledge of the position of the appendix and cecum during pregnancy.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1930, *42*, 465–477.

The author examined by means of opaque meals and enemas 53 pregnant women to determine the changes in position of the appendix and cecum and found that there was only a slight upward displacement. The appendix shadow was demonstrated in 50 per cent of the cases.

Ten women of the puerperal period were also examined, and here a roentgen visibility of the appendix was found in 80 per cent.

The amount of radiation on the surface of the skin during the entire examination amounted to only 40 r, no ill effects being observed either in mother or child.—*T. Leucutia.*

von Hecker, H., and Prévôt, R. Zur Röntgendiagnostik der hypertrophischen Gastritis. (On the roentgen diagnosis of hypertrophic gastritis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1930, *42*, 486–492.

The authors describe in detail two cases of hypertrophic gastritis in which a relief examination of the stomach revealed irregular coarse rugae. The differential diagnosis included residue of food particles, gastritis polyposa and chronic atrophic hyperplastic gastritis secondary to carcinoma (Konjetzny). The primary nature of the disease was established on the basis of the fact that repeated examinations extending over a period of several years failed to reveal any change in the appearance of the mucosal folds.—*T. Leucutia.*

Jacquet, Paul, and Gally, Léon. Le diagnostic radiologique de l'appendicite chronique. (The roentgen diagnosis of chronic appendicitis.) *Presse méd.*, Mar. 14, 1931, *39*, 376–379.

The authors previously reported the results of their investigations in the roentgen diagnosis of appendicitis. In the present article they wish to further elucidate certain points on the basis of newer experiences.

Localization of the Point of Tenderness. Since tenderness to palpation in the right lower quadrant may be due to several causes (pelvic celluli-

tis, neuralgia of the visceral plexus, pelvic adenopathy, etc.) a diagnosis of appendicitis should be made only if the point of tenderness is localized to the internal border of the cecum and if it strictly follows the displacement of the cecum during manipulation.

Ileocecal Delay of the Barium. Normally the barium column reaches the hepatic flexure six hours following the administration of the meal, only a minimal residue remaining in the ileum. In chronic appendicitis, a great part of the barium will be found in the terminal ileum. This is not due to stagnation as observed, for example, in obstructive lesions but simply to prolonged passage of the barium column through the cecum.

Ileocecal Spasms. The spasms form a nearly constant finding in chronic appendicitis. They may involve the cecum and the entire ascending colon or may be localized to the ileocecal region alone. In some instances the spasm is so pronounced that it leads to a conical or even pencil-shaped contraction of the cecum, giving a diverticulum-like appearance. In other instances, a deep incisure of the external border of the cecum is observed opposite the point of tenderness, not unlike the incisure of the greater curvature of the stomach opposite an ulcer. Occasionally the incisure may be so deep as to give the appearance of a false biloculation of the cecum.

Visualization of the Appendix. A barium-filled appendix at the six-hour examination is a rather rare finding, the filling occurring in most cases twelve to twenty-four hours after the ingestion of the barium meal. The filling is of diagnostic value only if associated with sensitiveness to pressure.

Perivisceritis. The existence of perivisceritis (Lane's bridge, Jackson's membrane, loose adhesions of the ileum, etc.) is debatable.

Concomitant Functional Disturbance of the Stomach. The gastric evacuation in chronic appendicitis not infrequently is irregular, anarchic and contradictory, leading to a veritable paradox: in spite of the hyperkinetic accelerated contractions, there is a large residue of the barium at the six-hour period. In a more general way, one may say that whenever the two right quadrants, upper and lower, present simultaneously functional disturbances, the site of the lesion lies most probably in the lower. In a very few instances, an arrest of the barium in the segments of the small intestine is observed, due to retrograde peristalsis.—*T. Leucutia.*

GUTMANN, RENÉ A. Indications respectives de la radioscopie et de la radiographie dans les maladies du tube digestif. (Respective indications of roentgenoscopy and roentgenography in diseases of the digestive tract.) *Presse méd.*, Feb. 14, 1931, *39*, 217–219.

The author discusses in detail the relative value of roentgenoscopy and roentgenography in the diagnosis of various lesions of the gastrointestinal tract such as duodenal ulcer, juxtapyloric ulcer, ulcer of the lesser curvature, pyloric stenosis, operated stomach, gastric carcinoma, cholecystitis and periduodenitis. He arrives at the conclusion that roentgenoscopy has its value especially in the functional diagnosis, while roentgenography is indispensable in the organic diagnosis.

There is no doubt that one may recognize at the roentgenoscopic examination very large ulcers, the majority of inoperable tumors, biloculations, stenosis, ptosis, aerophagy, malformations such as hernia, diaphragmatic eventrations, etc., and that one may be able to make a tentative diagnosis in ulcers of smaller size, in less extensive carcinomas and in cholecystitis, but in the early stage of most lesions, which really is the most important from the standpoint of treatment, no definite diagnosis can be made without the aid of roentgenography. In this respect, the author advises the use of serial films which must be of good quality and exactly localized to the area under examination. The modern roentgenographic study of the folds of the mucosa of the gastrointestinal tract is also of considerable help.

In conclusion, the author strongly condemns the attempt of many internists in trying to make gastrointestinal diagnoses on the basis of roentgenoscopic examination alone.—*T. Leucutia.*

DELREZ, L., and PARIS, M. Cholécystographie et rythme d'élimination par le foie de la tétraiodphenolphtaléine. (Cholecystography and the rhythm of elimination through the liver of the tetraiodophenolphthalein.) *Presse méd.*, Jan. 21, 1931, *39*, 97–99.

There are three theories for the explanation of the roentgen visibility of the gall-bladder in cholecystography: (1) the period of visibility depends on the amount of iodine elimination

through the liver; (2) the visibility depends on the concentration of the bile within the gall-bladder itself, and (3) the visibility depends on both.

The authors performed a series of experiments in 3 patients with cholecystotomy and choledochotomy by collecting the iodine containing bile alternatingly from the gall-bladder and from the ductus choledochus following the administration (per os or intravenously) of iodtetragnost Merck and arrived at the following conclusions:

1. The concentration of iodine in the hepatic bile depends very much on the mode of administration of the tetraiodophenolphthalein; it is incomparably less following the administration per os than by intravenous injection.

2. The rhythm of hepatic elimination of the iodine in different subjects who received the iodtetragnost by the intravenous route and under identical experimental conditions varies to a great extent in time and intensity. The maximum concentration in the cases observed was 3,149 mg., 955 mg. and 292 mg. per liter respectively, while the total amount eliminated in twenty-four hours amounted to 47.5 per cent, 22 per cent and 13.2 per cent respectively.

From a practical standpoint, this means that one must interpret with great caution the roentgen images in cholecystography: in some instances the gall-bladder shadow may appear visible at four to six hours following the injection and entirely invisible at the regular ten to eighteen hour period, while in others the time of visibility may be prolonged beyond that of the routine eighteen hour period. For this reason, a non-visualization of the gall-bladder between ten and eighteen hours must not be considered as absolutely indicative of a gall-bladder affection. It may be the result of a functional disorder of the liver, leading to a very rapid or unusually slow elimination of the iodine.—*T. Leucutia.*

GYNECOLOGY AND OBSTETRICS

Thomsen, Einar. Roentgen examination of the female urethra, specially in cases of prolapse and incontinence. *Acta radiol.*, Nov. 15, 1930, *11*, 527–536.

Roentgen examination of the male urethra has been systematically used of recent years but the method has not been used for the examination of the female urethra. The author describes two methods by which urethrograms of the latter may be made. Pictures are given which were taken by the lipiodol injection method. So far four classes of cases have been examined: (1) patients with perfectly normal and normally functioning genital organs; (2) patients with relative incontinence of urine without demonstrable prolapse but with slight descent of the vagina; (3) patients with distinct descent and prolapse but with the closing mechanism of the bladder functioning in a perfectly normal manner; (4) patients with marked prolapse and more or less severe incontinence.

The author shows that the normal female urethra at one point has a bend which has not hitherto been described and that a relative incontinence of urine is associated with straightening out of this bend.—*Audrey G. Morgan.*

GENITOURINARY SYSTEM

von Lichtenberg, A. Intravenous pyelography. *Radiology*, Dec., 1930, *15*, 664–669.

The author states that intravenous pyelography with uroselectan is indicated (1) in those cases in which cystoscopy, catheterization of the ureter and instrumental pyelography cannot be performed because of anatomic, pathologic or technical reasons; (2) in all cases of ureteral obstruction in which the contrast substance introduced by means of instrumental pyelography does not pass the point of obstruction, and (3) in those cases in which instrumental pyelography cannot be undertaken without risk to the patient. This last group should include those patients whom one wishes to spare the pain of catheterization and of whose condition one can obtain sufficient information through intravenous pyelography. Specifically, the intravenous method is applicable in patients suffering from stricture, severe bladder affections, hemorrhage, fistula, and in small children. It is applicable also in cases in which one hesitates to use the catheter, namely, in cases of acute and chronic inflammatory infections of the adnexa, in tuberculosis and in cases of prostatic hypertrophy.

A diagnostic film can be expected only in cases in which renal function is present, and the density of the shadow is dependent on the amount of function that exists. The shadow will be absent, faint or considerably delayed in severe bilateral infections of the kidneys, particularly those conditions associated with a damaged purulent parenchyma.—*J. D. Camp.*

Gabriel, Gerhard. Experimentelle Untersuchungen über die intravenöse Pyelographie bei pathologischen Zuständen der Niere. (Experimental study of intravenous pyelography in pathological conditions of the kidney.) *Acta radiol.*, Nov. 15, 1930, *11*, 500–504.

In order to study the value of intravenous injection of uroselectan as a means of making the urinary tract visible for roentgen examination, pathological changes similar to those occurring in man were produced in young rabbits by irradiation and operation. It was found that in cases of destruction of the kidney tissue and of inflammatory processes, either in the kidney parenchyma or in the pelvis, the contrast fluid showed the passages less distinctly and required a longer time to make them visible at all than in normal kidneys. In cases of pronounced pyonephrosis with obstruction of the ureter the contrast effect failed entirely. By temporarily closing the ureter good pictures of the renal pelvis can be obtained.—*Audrey G. Morgan.*

Swick, Moses. Intravenous urography by means of the sodium salt of 5-iodo-2-pyridon-N-acetic acid. *J. Am. M. Ass.*, Nov. 8, 1930, *95*, 1403–1409.

A brief history of intravenous urography is given, including the author's early experimental work with von Lichtenberg. The technical problems involved in determining the qualitative factors in secretion are considered in some detail. The technique of administration is outlined, the reactions mentioned, and the indications and contraindications briefly considered. Pyeloscopy by this method is satisfactory only when the function of the kidney is sufficiently good to provide dense shadows. Iodine is found in blood, stools, sputum and skin following injection.—*E. W. Hall.*

Jaches, Leopold. Intravenous urography (Swick method). *J. Am. M. Ass.*, Nov. 8, 1930, *95*, 1409–1412.

The Swick method of administration is employed and films made at necessary intervals, best results being obtained during the period from fifteen to sixty minutes after injection. No case of iodism has been observed. Both kidneys are visualized at once, anomalies are often shown that are missed by retrograde study, and the method is comparatively painless. The function of the tract is determined as well as its outline. Non-visualization at any given time may denote mere inhibition of renal function without permanent renal damage. Retrograde pyelography is not eliminated but is very necessary in many cases, such as in extreme impairment of kidney function in uremia.—*E. W. Hall.*

NERVOUS SYSTEM

Woltman, Henry W. The diagnosis of tumors involving the spinal cord. *J. Am. M. Ass.*, Nov. 8, 1930, *95*, 1398–1402.

The diagnosis of tumors involving the spinal cord depends chiefly on the patient's history and involves the duration, location and character of pain, disturbance in motility, sensibility and spincteric control. The examination of the spinal fluid is of value in differential diagnosis and roentgenogrphy may show occasional erosion of bone or calcium deposit but the injection of iodized oil is of little value as a rule and is irritating to the meninges. Tumors must be differentiated from inflammatory and posttraumatic conditions as well as from multiple sclerosis, syringomyelia and other degenerative diseases. Numerous diseases may give some symptoms simulating those of spinal cord tumor. Three illustrative cases are described.—*E. W. Hall.*

SKELETAL SYSTEM

Spies, J. W. Adenoid cystic carcinoma: Generalized metastases in three cases of basal cell type. *Arch. Surg.*, Sept., 1930, *21*, 365–404.

The author reviews the literature with special reference to the basal cell types of cutaneous epitheliomas and emphasizes the important differential diagnosis which is necessary to distinguish between the benign epithelioma adenoides cysticum of Brooke and Fardyce, cystic rodent ulcer, typical basal cell carcinoma as described by Krompecher and adenoid cystic carcinoma.

Krompecher's classification of a cutaneous and a non-cutaneous origin is also accepted by the author with realization that such division is not accepted by all pathologists.

The origin of tumors belonging to the adenoid cystic group is probably from the basal layer of the rete or from the sheath of a hair follicle, having a similar origin as the basal cell carcinoma, though it must be stated that tumors of sweat gland origin are distinctly different from the adenoid cystic epitheliomas, the former be-

ing due to a growth and cystic dilatation of the ducts rather than the sweat gland proper.

Tumors arising from both cutaneous and non-cutaneous sites, presumably from basal cells or their derivatives, possess unmistakable adenoid cystic features. Since these tumors may be classed as basal cell carcinomas there is a general tendency to minimize their lethal qualities. Their potential ability to widely metastasize and, in the case of the non-cutaneous origins most commonly found in the nose, antrum or soft palate, where easy extension is possible, makes an accurate diagnosis by biopsy and early and thorough treatment paramount. In no case has an unquestioned basal cell carcinoma metastasized, though lesions are found which in addition to basal cell elements also contain squamous products, and this type of cancer does metastasize.

In the group of cutaneous cases studied by the writer, no correlation could be made regarding sex, etiology or familial tendencies. The lesion was more commonly noticed in the 5th decade, with the 6th decade next in frequency. Pain was mild and infrequent. The distribution of the lesions corresponded to that seen in the usual types of basal cell carcinoma.

When the disease progressed, it was by local extension. The question as to whether the neoplastic cells actively grow into living bone, or whether they merely replace devitalized osseous tissue which has been eroded and atrophied through pressure and infection is an unsettled point. External radium irradiation was the treatment of choice, with satisfactory results so far as the actual preservation of life goes. However, there were many recurrences and in several cases it was necessary, because of the extent of the disease, to destroy tissue widely. Such complications could have been avoided if treatment had been instituted earlier.

In the non-cutaneous group, the 6th decade of life contained the majority of the cases. Again nothing was noticed that would suggest the cause of the disease. Ulceration was a prominent feature in this group though it was difficult to tell if the ulceration was spontaneous. Pain was a much more prominent feature than in the cutaneous group. The palate was the primary site in most of the cases, with the antrum and the mucosa of the cheek next in frequency.

The disease progressed by direct extension. The lesions primary in the palate usually entered the nose and antrum. The ones which began in the antrum and nose ordinarily invaded the mouth, orbit and ethmoids. The anatomic relations of the parts usually affected make this method of spreading easy and render the tumor dangerous.

Radium and surgical intervention were the methods of choice in treating these lesions. The duration of the treatment and the duration of observation were so often terminated by death of the patient that no definite conclusions can be drawn as to the results of treatment other than that the adenoid cystic carcinoma is a radiosensitive tumor.

The author presents a very interesting histological study of the specimens removed for bisopy.

The author reports 3 cases in detail in which widespread metastases were found and in each case the microscopic examination of the autopsy specimens was adenoid cystic basal cell carcinoma, a subdivision of the basal cell group and an entirely different lesion from the benign skin disorder known as adenoid cystic epithelioma or Brooke's disease.—*F. K. Alexander.*

Levin, Isaac. Skeletal metastasis in carcinoma of the thyroid. *Am. J. Path.*, Sept., 1930, *6*, 563–572.

Following carcinoma of the prostate and of the breast, carcinoma of the thyroid most frequently metastasizes to the skeleton. Berard and Dunet found the most frequent sites of the metastases to be the skull and vertebrae. A simple colloid goiter, presenting a structure that usually remains harmless for years, may give rise to metastatic tumors. These secondary tumors may acquire the characteristics of malignancy though the primary tumor remains benign.

The author gives a brief survey of the mechanism of formation and pathogenesis of metastasis in carcinoma generally. An adequate explanation for the predilection of certain types of carcinoma to metastasize to bone has never been given. Von Recklinghausen maintained that the formation of metastases in the bone is due to the fact that the veins and capillaries of the bone marrow have thin walls, and are not collapsible. When one considers bone metastases from carcinoma of the uterus and carcinoma of the prostate, two organs having nearly the same vascularization and anatomical relations, it seems incredible on the basis of von

Recklinghausen's theory that Kaufmann should have found skeletal metastasis in carcinoma of the uterus in only 3.03 per cent of cases as compared to 66 per cent in carcinoma of the prostate. The opinion of Lubarsch that the difference in the relative sizes of the cancer cells and of the minute blood vessels of an organ influence the formation of metastases, is also hardly tenable. The bone marrow contains blood vessels of a sufficiently large caliber to admit the lodgment of a cancer cell of any size.

The author believes in the conception that while tumor emboli are transported everywhere with the same ease and find lodgment in any part or organ of the body, they nevertheless find better soil for development in certain organs where they develop into metastatic tumors, while in other less favorable organs they are destroyed.

Bone tissue is well suited for the study of the minute changes occurring under the influence of tumor growth. Two classes of metastatic bone lesions are generally recognized; osteoplastic, characterized by the production of new bone, and osteoporotic, in which bone tissue is destroyed. As the result of microscopic study the writer found that both conditions were generally present side by side. The difference in the gross appearance is due to the predominance of one or the other condition.

The mechanism of the bone destruction or osteoporosis has been variously conceived by different investigators. Von Recklinghausen and others believed that osteoporosis in skeletal carcinoma may take place without the aid of special cells. Goetsch believes that the cancer cells act as osteoclasts, while Axhausen maintains that the small elongated mononuclear connective tissue cells frequently found close to the walls of the laminae are special osteoclasts derived from the cancer stroma. As the result of his studies, the writer believes that the tumor itself, by the aid of its formed elements, first destroys the bone, and then grows by occupying the space so formed.

Likewise the mechanism of the new bone formation is also under dispute. Von Recklinghausen claims that it is due to a hyperemia described by him as occurring around tumor emboli; Askanazy thinks that the metastasis at first produces osteoporosis which is followed by a bone necrosis. The necrotic bone then acts as a foreign body stimulating new bone formation: Wolff and Kaufmann are of the opinion that cancer cells may act directly as osteoblasts. The writer believes that some unknown chemical irritant emanating from the cancer cells acts on the old bone tissue and stimulates its proliferation.

Thus, two processes always take place side by side. On the one hand, the tumor destroys the normal bone tissue; on the other hand, the remaining osseous tissue proliferates and creates new bone. The latter is quite probably an attempt at self defense. The new bone tissue may compress and destroy the cancer cells.

It is often difficult to differentiate morphologically between a benign and a malignant tumor of the thyroid. A small group of cells of a normal thyroid or goiter may become malignant. The thyroid or goiter offering an unfavorable soil suppresses the growth of these malignant cells. Some of these cells, however, may be transported to the skeleton where they find more favorable soil for their development. In consequence large metastatic tumors develop. Cases in which the primary growth in the thyroid is quite insignificant while the metastatic lesions in the skeleton dominate the clinical picture are not uncommon. Three such cases are reported. In all the primary condition in the thyroid was overlooked.

Whenever there is a diagnosis of malignant tumor in the skeleton, single or multiple, search for a primary lesion elsewhere must be made. In the female, next to the breast, the thyroid must be thought of; in the male, next to the prostate, the thyroid must be considered.—*Karl Kornblum.*

Hsieh, C. K. Echinococcus involvement of the bones: report of a case, with x-ray examination. *Radiology*, June, 1930, *14*, 562–570.

In general, the roentgen signs of bone echinococcus can be divided into two groups, the early and the advanced. The early stage is represented by irregular absorption or rarefaction of bone, which is usually taken for osteomyelitis or tuberculosis as in the cases of Harris. In the long bones, the involvement is most often met with in the ends of the shaft. The destruction may remain mild and latent for years. The advanced stage presents extensive cystic destruction, with the changes often interpreted as myeloma, osteitis fibrosa cystica, or metastatic neoplasm. The characteristic cystic destruction is well represented by the roentgenograms of the case reported and by the specimen of the

bony framework of Corlette's case. Between the two extremes all gradations of destruction may be encountered. Dew emphasizes the absence of subperiosteal thickening and bony reaction as an important diagnostic feature. He also calls attention to the lack of expansion of the bone, the absence of pain, the extremely slow progression, and the age of the patient. The infection often occurs in childhood but generally is not detected until later age, because of its slow development. Pathological fracture is usually present in advanced cases and sometimes occurs early. The pelvis, vertebrae, humerus, tibia, and femur are most often involved, the order of frequency being that in which they are mentioned.—*J. D. Camp.*

Imbert. Un cas de myosite ossifiante progressive. (A case of progressive myositis ossificans.) *Bull. et mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 467–470.

A very unusual case of myositis ossificans, involving all the muscles of the right shoulder and leading to nearly complete mummification, is described in a man who fifteen years previously suffered an injury to that shoulder, resulting in complete ankylosis of the scapulohumeral articulation. A roentgenogram is reproduced to show the condition.

It is the author's contention that the progressive ossification of the muscles is the result of circulatory disturbance brought about by the trauma to the shoulder.—*T. Leucutia.*

Kehrer, E. Zum röntgenologischen Nachweis der Hypertorsion in der kindlichen Halswirbelsäule. (Roentgen demonstration of hypertorsion in the child's cervical spinal column.) *Strahlentherapie*, Sept. 2, 1930, *37*, 609–618.

In the fetus and new-born infant there is extraordinary mobility of the cervical spinal column and torsion of the head is possible to as much as 135°. Warnekors' Roentgen Atlas gives a picture of such extreme torsion. The author describes and gives roentgenograms of 3 cases. Warnekors says that this hypertorsion is caused by pressure from the fundus but the author holds that is must be caused by external mechanical factors and cannot be caused by the movements of the child itself or contraction of the uterus from the fundus. He thinks that in placing the patient on the roentgen table and changing her from a dorsal to a lateral and then an abdominal position the table may exercise pressure on the child if the walls of the abdomen are flabby and the walls of the uterus thin. In the transverse position this hypertorsion of the head is not particularly dangerous for any skilled obstetrician will be able to turn the child's back and occiput before extracting it so that they face the anterior wall of the uterus and pelvis. But in skull presentation and in deflexion when the head has entered the pelvis and there is a hypertorsion of 135° the blood vessels of the neck may undergo torsion or traction on passage of the head and shoulder through the vulva which causes asphyxia and if not quickly corrected may threaten life.—*Audrey G. Morgan.*

Pondé, Adriano, and Silveira, José. Anomalie de la ceinture scapulaire. (Anomaly of the scapular girdle.) *Rev. sud.-am. de méd. et de chir.*, Feb., 1931, *2*, 163–167.

One of the most interesting and rarest anomalies of the shoulder girdle is the coracoclavicular articulation. Poirier, who observed the anomaly in 3 of 10 cadavers, thought the condition to be quite common, but the authors in a series of 3,300 roentgen films of the shoulder were able to discover only one single case. This case is discussed in detail and illustrated with roentgenograms and a diagram. The articulation is formed between the inferior aspect of the clavicle at the junction of the middle and outer thirds, and the posterior aspect of the coracoid process of the scapula. Concerning the etiology of the process, the authors endorse the theory of Frassetto, according to which the abnormal articulation is the result of a partial ossification of the ligaments uniting the clavicle and the coracoid process. Due to limitation of the movements in the shoulder joint, the condition predisposes to fracture of the surgical neck of the humerus.—*T. Leucutia.*

Porro, N. Sulla sindrome Malacica del semilunare-Morbo di Kienböck. (Malacia of the semilunar bone—Kienböck's disease.) *Arch. di radiol.*, 1930, 6, 690–712.

Six cases of softening of the semilunar bone are described. This disease generally occurs in patients of from seventeen to thirty years of age. It is about twice as frequent in women as in men, probably on account of the greater delicacy of their bones. It generally occurs in persons otherwise in good health; there is usually

no history of tuberculosis, syphilis or trauma. Generally without any apparent cause the patient begins to have pain in the wrist, particularly on the dorsal surface over the semilunar bone; the pain is more intense on movement of the hand on the forearm, particularly flexion. It stops on rest and is worse in the morning on first moving the hand. Sometimes there is slight swelling of the back of the wrist, rarely redness and local heat. There is crepitation on flexion and extension.

The roentgen picture shows the bone flattened vertically; sometimes it is reduced to a third of its normal volume. The bone has lost its semilunar form and is irregularly rectilinear and flat. Its surfaces are irregular, rough and dentate; the lower end of the radius is almost always normal. The flattening of the semilunar causes a slight shortening of the wrist. The structure of the bone is greatly changed. It no longer shows the normal trabeculation but is dense and sometimes ivory-like, giving a shadow almost as dense as that of metal. Generally the lesion is only in one hand, though some bilateral cases have been reported.

The disease from which it most frequently has to be differentiated is tuberculosis. Two of the author's cases were sent to him to confirm a diagnosis of tuberculosis. Differentiation is possible from the fact that there is no tendency to suppuration and the condition can generally be cured by rest. The roentgen picture is also different.

The milder cases recover with rest alone. Sometimes however pathological fractures take place in bones with this disease and sometimes bone processes develop on the edges and surfaces of the bones and in these cases arthritis deformans may result. In some cases immobilization with plaster is necessary and in very severe cases in which the pain and weakness persist some authors recommend extirpation of the bone.—*Audrey G. Morgan.*

Dale, T. Skelettveränderungen bei einem Falle von chronischem Empyem. (Changes in the bones in a case of chronic empyema. *Acta radiol.*, Nov. 15, 1930, *11*, 537–546.

The author describes a case of chronic empyema with acute painful swelling of the hands and feet accompanying pregnancy. A roentgen examination made four years after these last-named symptoms began showed general ossifying periositis of the long bones, a destructive process in the distal end of the radius and slight hyperplasia of the first and second phalanges of the four ulnar digits. Along the distal edge of the terminal phalanges of the fingers and toes were small rosette-shaped proliferations. After the patient had undergone an operation and had been cured of her empyema the swelling and pains in her hands and feet rapidly disappeared. Roentgen examination about one year after the operation showed no change in the periostitis of the long bones. The destruction of the radius, the hyperplasia of the proximal and middle phalanges of the fingers and the proliferations on the terminal phalanges of the fingers and toes had disappeared and the roentgen picture of these parts was now normal.—*Audrey G. Morgan.*

Genner, Viggo, and Boas, Harald. A case of generalised osteitis deformans (Paget) with secondary malignant degeneration. *Acta radiol.*, Sept. 30, 1930, *11*, 398–410.

The authors briefly describe the clinical characteristics of osteitis deformans on the basis of the first case reported by Paget. They also describe the complications, the pathologico-anatomical and roentgen changes, the various theories concerning the etiology of the disease and discuss the difficulties of its differentiation from other bone diseases, particularly Recklinghausen's osteitis fibrosa and from certain bone tumors.

They then report a typical case in a man aged fifty-one. He had had the disease for about thirty years and it had not affected his general health or ability to work. It was not discovered until he was admitted to the hospital for a swelling of his right shoulder, the result of an injury which he had sustained a few weeks before. Roentgen examination then showed that the swelling was due to a malignant growth in the bone tissue there and that he was suffering from a generalized form of Paget's osteitis deformans with typical malformation of some of the bones, especially those of the legs (saber legs). He died a few weeks later as a result of the development of a second malignant tumor and autopsy confirmed the clinical and roentgen diagnosis, showing extensive sarcomatous destruction of the right scapula, clavicle and part of the head of the humerus with large hemorrhagic tumor masses. In addition to that the patient had syphilis acquired when he was eighteen years old. It had been poorly treated

and the Wassermann reaction was still strongly positive. The patient was very deaf during the last few months of his life, evidently as a result of the osteosclerosis which is characteristic of the disease.—*Audrey G. Morgan.*

Conte, Ettore. Considerazioni intorno ad alcuni casi di osteodistrofia deformante (morbo di Paget). (Some cases of deforming osteodystrophy—Paget's disease.) *Radiol. med.*, Aug., 1930, *17*, 968–986.

The author first describes a case in a man of forty who had a fracture of the patella from trauma. The fracture had recurred in spite of metal wiring. Roentgen examination showed changes in other bones of the skeleton, particularly the skull. It was beyond doubt a case of Paget's deforming osteodystrophy which had caused changes in the femurs, the pelvis and both humeri and the last lumbar vertebrae in addition to the ones already mentioned. It differs from the classical cases in the fact that the vertebrae were only slightly affected and there were no marked signs of compression of the diaphyses of the tibia. Although it had been six years since the first signs of the disease began the patient's appearance was absolutely normal except for the skull and a slightly limping gait because of the failure of the fracture of the patella to heal. The patient attributed his disease to the trauma but it probably antedated that and the trauma caused a fracture of a bone that was already diseased. The bones of the skull were very thick and the cranium appeared to be pushed down over the spinal column. This is due to the weight of the skull and the plastic softening of the bones of the base.

Two cases in syphilitics are then described and the relation between syphilis and Paget's disease discussed. He decides that they are two different diseases and that in his case the syphilis occurred first and the osteodystrophy developed in the lesions caused by the syphilis.—*Audrey G. Morgan.*

Inglis, John. A case of osteogenesis imperfecta infantilis. *J. Am. M. Ass.*, Oct. 25, 1930, *95*, 1262–1263.

This male child, born of an apparently healthy mother, showed at birth seventy-four distinct skeletal fractures with attempts at intrauterine healing. As in the usual case the child died shortly after birth. Autopsy and roentgen findings were not unusual except for the osteogenesis imperfecta with the multiple fractures. Five additional cases are mentioned as having been reported in the literature.—*E. W. Hall.*

Freund, Ernst. Zur Deutung des Röntgenbildes der Perthesschen Krankheit. (The roentgen appearance of Perthes' disease.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1930, *42*, 435–464.

The author made a detailed study of the roentgen appearance of Perthes' disease by taking roentgenograms regularly at three month intervals. The series included 29 cases between four and twelve years of age, 24 (83 per cent) of which were boys and 5 (17 per cent) girls. In 26 the lesion was unilateral (14 right and 12 left) and in 3 bilateral. A direct traumatic etiology was demonstrated in only 10 cases.

It was found that the course of the disease in the uncomplicated cases is quite characteristic. It is the author's opinion that the primary provoking factor lies in a traumatic compression of the epiphyseal nucleus which, as is known, is entirely surrounded by cartilge. The compression results in an aseptic necrosis of the head of the femur and not infrequently of the proximal portion of the femoral neck. In a few instances a typical fracture line may appear in the subchondral spongiosa running parallel with the contour of the head. In the more advanced cases the compression of the necrotic epiphysis may result in a marked deformity and thickening of the head and neck of the femur.

Most of the roentgen changes are due to the regenerative process within the necrotic epiphysis and are by no means pathologic. The regeneration occurs in a characteristic manner and it lasts in the uncomplicated cases in which early immobilization is applied for a period of 1½ to 2 years. It begins with a connective tissue granulation from the periosteum near the epiphyseal border leading first to osteoporosis and later to zones of increased transparency, especially of the median and lateral portions of the head of the femur. In a large number of cases, there is, in addition to this marginal regeneration, also a central regeneration beginning at the fovea capitis from the blood vessels of the ligamentum teres. In this latter instance a zone of increased transparency may be demonstrated leading from the fovea capitis towards the center of the head of the femur and dividing it into a smaller median and a large

lateral portion. In case the marginal regeneration has progressed further than the central regeneration, one may encounter concomitantly areas of new bone formation along the borders and zones of necrosis in the center, this resulting in the so-called "fragmentation." During the later stage of regeneration, the head assumes a characteristic deformity not infrequently leading to subluxation which consequently is not a congenital anomaly as usually thought, but a secondary complication of the course of repair. Occasionally a deformity of the neck of the femur is also observed due to disturbance in the endochondral ossification.

It follows from the above that the most rational method of treatment of Perthes' disease consists in a rigorous immobilization in the earliest stages of the process, this not infrequently resulting in a complete restitutio ad integrum.—*T. Leucutia.*

Phemister, D. B., Brunschwig, Alexander, and Day Lois. Streptococcal infections of the epiphyses and short bones. *J. Am. M. Ass.*, Oct. 4, 1930, *95*, 995–1002.

Bacteriologic studies of biopsy material were made from 6 cases of epiphyseal disease and related conditions, namely, Köhler's disease of the scaphoid, Legg-Perthes' disease of the hip, and Kienböck's malacia of the os lunatum. In 4 of the 6 cases streptococci were grown from removed fragments, 2 remaining sterile. It is suggested that streptococci play an important rôle in the etiology of these diseases, the exact mechanism remaining undetermined.—*E. W. Hall.*

Hanson, Malcolm B., and Fenger, I. Healing in bone tuberculosis. *Radiology*, Sept., 1930, *15*, 374–376.

The method of healing in any infection of a joint in which there has been bony destruction may be primarily classified under two heads: (1) by fibrous union or replacement of eroded bones and cartilage by connective tissue; (2) by new bone formation in and about the joint. In this article only that class in which there is demonstrable new bone formation during the stage of repair is considered.

Cofield, in 1922, called attention to "bony bridging in tuberculosis of the spine." The authors' experience corresponds with his, and they have found that not infrequently quite extensive new bone formation is seen in the repair of joint tuberculosis in cases in which there have been no communicating sinuses, with secondary infection. In their experience it has also been noted that healing by production of osseous tissue is more prevalent in tuberculosis of the vertebrae than in hip or sacroiliac involvement. About 15 per cent of Hanson and Fenger's cases of Pott's disease have demonstrable new bone formation during the stage of healing.

The differential diagnosis from a roentgen standpoint between tuberculous joints, arthritis deformans, and some cases of septic joint disease must occasionally lie in the appreciation of secondary findings as, for instance, presence of paravertebral abscess and presence of accompanying pulmonary tuberculosis.—*J. D. Camp.*

Camplani, Mario. Ulteriore contributo alla conoscenza delle alterazioni scheletriche nella tabe dorsale. (Changes in the skeleton in tabes dorsalis.) *Radiol. med.*, Sept., 1930, *17*, 1048–1053.

A man, aged fifty-six, had had syphilis about twenty-five years before and had had several irregular periods of treatment, the last in 1925. At that time he was admitted to the hospital for fracture of the right leg. On the present admission he complained of pain in the lower limbs and back. Physical examination showed tabes dorsalis. Roentgen examination of the right leg showed a large callus of the internal malleolus with a lacunar structure. The tibia and fibula appeared to be fused into one exuberant bone. There were multiple osteophytes and a curvature of the leg with the concavity inward. The picture of the spine showed changes in the last dorsal and first lumbar vertebrae. There were beak-shaped structures on the bodies of the vertebrae and intervertebral bridges, particularly marked between the 11th and 12th dorsal. In the anteroposterior projection the body of the 12th dorsal was somewhat flattened vertically. In the latero-lateral projection the body of the 12th dorsal was seen to be eroded, having lost almost a third of its anteroposterior diameter; the body of the 11th dorsal was eroded and flattened and the first lumbar was affected by the same process but not to so great a degree. The bodies of the first, second and third lumbar vertebrae showed typical beak-shaped structures and intervertebral bridges. The picture showed both destructive and productive changes which could

not be differentiated from those of spondylitis deformans.—*Audrey G. Morgan.*

Alajouanine, Th., and Petit-Dutaillis, D. Le nodule fibro-cartilagineux de la face postériure des disques intervertébraux. (The fibrocartilaginous nodule of the posterior surface of the intervertebral discs.) *Presse méd.*, Dec. 6, 1930, *38*, 1657–1662 and Dec. 20, 1930, *38*, 1749–1751.

The authors describe in detail two unusual cases of radiculomedullary compression due to fibrocartilaginous nodules of the posterior aspect of the intervertebral discs. Briefly, the following findings have characterized the cases.

Case 1. Left-sided lumbosciatic pain which at first occurred only occasionally but later became nearly continuous, and which at the end of four years was associated with motor, sensory and sphincteric disorders. Hemisyndrome of the left cauda equina. Slight albuminocytologic dissociation of the spinal fluid. Arrest of the lipiodol between the fifth lumbar and first sacral segment. Lumbarization of the first portion of the sacrum, with left sacralization. Laminectomy. Removal of the fibrocartilaginous nodule from the intervertebral disc between the fifth lumbar and the first sacral. Rapid and complete healing.

Case 2. Progressive left-sided lumbosciatic pain which at the end of three years became associated with motor, sensory and sphincteric disorders. Hemisyndrome of the left cauda equina. Slight albuminocytologic dissociation of the spinal fluid. Negative roentgen findings with negative result of the lipiodol injection. Laminectomy. Removal of the fibrocartilaginous nodule from the posterior aspect of the intervertebral disc between the third and fourth lumbar segments, pressing on the sacral roots. Incomplete healing.

In connection with these two cases, the authors discuss in detail the pathology, etiology, symptomatology and treatment of the fibrocartilaginous nodules originating from the posterior aspect of the intervertebral discs, and pressing on the spinal cord.

A review of the literature revealed that 21 similar cases had been described, 10 of which occurred in the cervical, 3 in the dorsal and 7 in the lumbar region. In nearly all instances the site of the lesion was laterally from the midline, resulting in a hemilateral syndrome. Contrary to the opinion of the majority of neurosurgeons, it was found that the nodules removed did not represent ,chondromas, fibrochondromas, or chordomas, but that they were simple cartilaginous formations resembling the structure of the intervertebral discs. They were always of small volume and implanted on the posterior aspect of the intervertebral discs. Androe, who made a detailed study of the subject, advanced two theories for the pathogenesis of these formations: they may be either the result of a posterior expansion of the intervertebral disc due to condensing osteitis of the central portion of the disc or the result of a hernia of the nucleus pulposus through a Y-fissure at the posterior part of the vertebral bodies. In the latter instance a simple trauma or an alteration (degeneration) of the cartilaginous plates may form the provoking factor.

The diagnosis is based on the following signs: (1) Neurologic, (*a*) root syndrome: pain, paresthesia, hypotonia, abolition of the reflexes, anesthesia or hyperesthesia; (*b*) medullary syndrome: motor-sensory disturbances similar to those observed in the Brown-Séquard syndrome, paraplegias, cord pain, paresthesia, fibrillar twitchings, localized, atrophy, etc. (2) Biologic signs of compression: albuminocytologic dissociation, arrest of lipiodol, negative roentgenography of the spine.

The evolution of the disease at first is very slow but following the appearance of the objective signs, it becomes very rapid. In both cases observed by the authors for a period of three to four years, there was only pain, but later signs of compression rapidly developed.

The prognosis depends, of course, upon whether the diagnosis is made early in the first stage of the disease, or after the signs of compression have already set in.

The treatment is surgical and consists in the removal of the cartilaginous nodule.—*T. Leucutia.*

Perotti, D. Contributo allo studio del significato di alcune particolari alterazioni dei corpi vertebrali. (Study of the significance of some changes in the bodies of the vertebrae.) *Radiol. med.*, Aug., 1930, *17*, 932–940.

The author describes and presents roentgenograms of 7 cases of spondylitis in which the roentgenograms showed irregularities in the boundary planes of the bodies of the vertebrae or indentations in the shape of cupolas caused by Schmorl's cartilage nodules. Schmorl first

described these nodules, which he attributed to the intervertebral discs penetrating the vertebrae because the resistance of the cortex had been decreased by some pathological process. The author thinks the nodules are caused by tuberculosis, representing either an initial stage of caries of the vertebrae, or slight lesions immediately circumscribed by an energetic reaction on the part of the surrounding bone. Enlargement of the intervertebral spaces with irregularity of the boundary planes or cartilaginous nodules that have not yet indented the planes are among the earliest symptoms of spondylitis.—*Audrey G. Morgan.*

Mayers, Laurence H. A concept of arthritis. *Radiology*, Oct., 1930, *15*, 487–494.

Mayers has come to the conclusion that the disease known as arthritis is a chronic infective condition, in which the joint manifestations are the end-products of a long period of intoxication, which intoxication results from an infective process. He considers chronic infective arthritis a non-selflimited disease, comparable only to syphilis and tuberculosis. Since neither tuberculosis, syphilis nor arthritis can be cured by attacking the affected anatomical systems, the diseases being general, the vaccine treatment seems to be the most logical method of combating arthritis. The value of vaccine treatment depends upon whether or not the bacterium used is pathogenic for the individual.—*J. D. Camp.*

Bachmann, A. Ein Beitrag zur Spondyloarthritis ankylopoetica. (A contribution to ankylopoetic spondylarthritis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1930, *42*, 500–509.

A study of 3,201 roentgenograms of the spine revealed ankylopoetic spondylarthritis in 66 cases (2 per cent) and spondylopathia deformans in 674 cases (about 18 per cent).

Four cases of ankylopoetic spondylarthritis in which the ankylosis extended in addition to the intervertebral articulations, also to other joints of the body (e.g., costovertebral, sacroiliac, coxofemoral articulations, etc.) are described in detail.

Forty-one cases were examined with regard to etiology, sex and age. It was found that trauma occurred in 6 per cent, whereas insidious rheumatism or other infections constituted the etiological factor in 85 per cent of the cases. In 90 per cent the male and in 10 per cent the female sex was affected. The majority of cases occurred between the ages of thirty and fifty and only in 16 per cent between twenty and thirty.—*T. Leucutia.*

Coste, F., and Lacapére, J. Grands syndromes du rhumatisme chronique des jointures. Les arthrites. (Grand syndromes of chronic rheumatism of the joints. The arthrites.) *Presse méd.* Mar. 11, 1931, *39*, 353–356, and Les arthroses. (The arthroses.) *Presse méd.* Mar. 21, 1931, *39*, 417–418.

The various textbooks use a rather complicated classification for the various forms of articular rheumatism. The authors suggest the following two general divisions: (1) arthritis and (2) arthrosis.

(1) The roentgen appearance of arthritis varies according to the stage of involvement. At the beginning, there is only an inflammatory reaction of the bones around the joint, the osteoporosis being very discrete. Later, the decalcification progresses, the epiphyses become blurred, the cartilage shows a tendency to disappearance and the interarticular space narrows. In a still later stage, the progress of the lesion leads to fusion of the articular surfaces, to loss of the interarticular space and to marked decalcification of the adjacent bones. The terminal stage is represented by complete ankylosis.

Clinically, the term arthritis includes all forms of inflammatory conditions of the articulations. Of 109 cases examined by the authors, in 21 the etiologic cause was determined with certainty, in 28 it remained doubtful and in 60 no etiologic factor could be ascertained. The cases with definite etiology consisted chiefly of post-rheumatic, gonococcic, syphilitic and post-scarlatinal arthrites. In the indefinite group, deforming progressive polyarthritis was encountered most frequently. All mono- or oligo-articular forms with inflammatory symptoms were placed in this latter group, especially when they were confined to the vertebral column, as, for example, rhizomelic spondylosis, which is also called "ankylopoietic" arthritis.

(2) The roentgen appearance of arthrosis is characterized chiefly by marked deformity of the contours of the bones resulting in osteophytes, spurs, parrot-beak formations, etc., there being absence of decalcification.

The forms included under this division are (*a*) the arthritis sicca (lipo-arthritis) of the knee, hip and occasionally of other joints; (*b*)

the lumbar osteophytic rheumatism; (*c*) the nodular rheumatism, also called Heberden nodules of the hands, etc., and (*d*) the corresponding deformities of the feet and toes.

The authors also discuss in great detail the etiological, clinical, biological and anatomical factors in both the arthrites and arthroses.

In conclusion, they criticize the indiscriminate use of the term "rheumatism" suggesting that it should be reserved for the designation of "acute articular rheumatism" or so-called Bouillad's disease, forming a sub-variety of arthritis.—*T. Leucutia.*

Ley, Jacques, and Snoeck, J. J. Polyarthrite symétrique primitive à évolution chronique progressive et destructive chez des soeurs jumelles. (Primitive symmetrical polyarthritis of chronic, progressive and destructive evolution in twin sisters.) *Presse méd.*, Feb. 21, 1931, *39*, 264–268.

The authors recently had the opportunity to observe a rather unusual form of polyarthritis which is variously called in the literature chronic primary polyarthritis (Assmann), primary chronic progressive articular rheumatism (Pribram) or primary chronic progressive polyarthritis destruens (Hoffa and Wollenberg).

The condition occurred in twin sisters twenty-two years old, having its onset in the first at the age of eleven and in the second at the age of eighteen. The clinical picture, briefly, consisted in the successive symmetrical involvement of the small articulations first, and of the larger articulations later, the evolution being of a chronic progressive character and leading ultimately to ankylosis.

Roentgenologically, the changes were similar in the two cases except that they appeared more pronounced in the first, due no doubt to the longer duration of the disease. They consisted in a marked osseous atrophy of the epiphyses and of the short bones. The osteoporosis was especially pronounced in the bones of the hands and wrists where, in addition, there was evidence of destruction or diminution of the articular spaces, this resulting in complete synostosis. The knees presented, likewise, extreme decalcification with deformity of the epiphyses and disappearance of the articular surfaces. The coxofemoral articulations, which clinically appeared to be uninvolved, revealed an irregularity of the contour of the cartilages with decalcification and a tendency towards synostosis. Roentgenograms taken at various intervals later showed a slow but definite progress in all lesions.

The diagnosis was based especially on the following three factors: (1) the simultaneous involvement of the homonym articulations, of the smaller first and of the larger later; (2) the slow evolution associated occasionally with slight attacks of fever, and (3) the enlargement and deformity of the epiphyses, the thickening of the articular capsule and the diminution or complete disappearance of the interarticular space, with extreme osteoporosis of the adjacent bones.

In discussing the etiology, the authors express the opinion that the condition is neither familial nor hereditary. In the cases mentioned it most probably was the result of ovarian disturbance (insufficiency of the ovary). The possibility of contagion can be excluded through the fact that the two sisters were separated from early girlhood, growing up under different surroundings, and that other brothers and sisters in actual contact have failed to develop the disease.

Various therapeutic methods were tried, such as opotherapy, helio-hydro-electro-mechanotherapy, administration of salicylates, etc., all without noticeable result. Thus the prognosis, while not fatal quoad vitam, must be regarded as very reserved.

The condition is exceedingly rare.—*T. Leucutia.*

Fischgold, H. Sur un cas de malformation de la plante des pieds. (A case of malformation of the foot.) *J. de radiol. et d'électrol.*, Dec., 1930, *14*, 641–642.

This is a very brief case report (illustrated with photographs and roentgenograms) of an unusual malformation of the left foot in a boy seven months of age. There were 9 toes, the fifth and sixth forming partial synostosis. The roentgenograms revealed one astragalus, one calcaneus, 2 cuboids, double third cuneiform, 8 metatarsals and the phalanges of 9 toes, those of the fifth and sixth forming synostosis. It is interesting that the mother also had a synostosis of the third and fourth toes on both sides. Whether there is any correlation between the malformation of the child and the synostosis of the mother is a debatable question.—*T. Leucutia.*

BLOOD AND LYMPH SYSTEM

Horton, Bayard T., and Craig, Winchell McK. Evidence shown in roentgenograms of changes in the vascular tree following experimental sympathetic ganglionectomy. *Arch. Surg.*, Oct., 1930, *21*, 698–701.

The constant changes that follow sympathetic ganglionectomy and ramisectomy have been attributed clinically to the increased flow of blood to the extremities as shown by physiologic observations with the calorimeter and thermocouple.

The authors did four experiments in dogs, and found definite evidences of vasodilatation in the arterial tree of the hind extremity following interruption of the sympathetic innervation by lumbar sympathetic ganglionectomy and ramisectomy. Changes were not observed in the arterial tree following periarterial sympathetic neurectomy. They made roentgenograms after the injection of mercury into the arterial tree, and their observations are in accord with the clinical observations in man that have been made at the Mayo Clinic.—*E. P. Pendergrass.*

do Amaral, Zephirino. Volumineux anévrysme de l'artère ischiatique. Anévrysmographie par l'iodure d'urée. (Large aneurysm of the ischiatic artery. Aneurysmography by means of iodated urea.) *Rev. sud.-am. de méd. et de chir.*, Feb., 1931, *2*, 155–162.

A rather unusual case of aneurysm of the right gluteal region originating from the ischiatic artery is described in a negro aged forty-nine. The injection of iodated urea into the aneurysmal sac led to excellent roentgen visualization of the condition.

In connection with this case, the author discusses the frequency, clinical diagnosis and the treatment of aneurysms in the gluteal region.—*T. Leucutia.*

ROENTGEN AND RADIUM THERAPY

Pohle, Ernst A., and Wright, Cecil S. Studies of the roentgen erythema of the human skin. III. Macroscopic and skin capillary changes after combined exposure to roentgen rays and ultra-violet rays. *Radiology*, April, 1930, *14*, 351–359.

The combined effect of roentgen rays and ultraviolet rays was studied on the skin of rats and on human skin. Three qualities of roentgen rays were used; an air-cooled quartz mercury vapor lamp served as source for the ultraviolet radiation. The roentgen doses are expressed in r-units; the output of the ultraviolet lamp was controlled by a calibrated photo-electric cell.

All experiments led to the conclusion that ultraviolet radiation enhances the effect of roentgen rays on the skin, at least temporarily. There is no indication of a true antagonistic action. The conclusions of previous investigators are, therefore, supported. It is inadvisable to use ultraviolet rays as emitted by a quartz mercury vapor lamp to counteract the effect of roentgen rays on the skin. Ultraviolet rays do not seem to hasten the healing of the acute roentgen ulcer if applied immediately after its appearance.—*J. D. Camp.*

Butler, Carlos. Epithélioma cutané, considérations sur 1302 cas traités à l'Institut de de radiologie. (Cutaneous epithelioma, consideration of 1302 cases treated at the Institute of Radiology.) *Rev. sud-amer. de méd. et de chir.*, Dec., 1930, *1*, 1265–1266.

The author gives a statistical analysis of 1302 cases of skin epithelioma treated under his direction at the Institute of Radiology, University of Montevideo. Of these, 47.3 per cent were of the basal cell type; 44.2 per cent of the squamous cell type and 8.5 per cent of the intermediary or mixed type; 62.9 per cent of the lesions occurred in men and 37.1 per cent in women.

The methods employed for treatment were curie therapy, roentgen therapy, radiosurgery and diathermic coagulation, or a combination of several. The best results were obtained by curie therapy. Of all the cases, in 66.7 per cent a complete healing, and in 25.6 per cent an amelioration was obtained. Of the 597 cases cured, 306 have passed the five year, 112 the ten year, and 18 the fourteen year period.—*T. Leucutia.*

Delherm and Morel-Kahn. La roentgenthérapie dans le traitement de la syringomyélie. (Roentgen therapy in the treatment of syringomyelia.) *J. de radiol. et d'électrol.* Sept., 1930, *14*, 481–485.

Sixteen cases of syringomyelia have been treated by the authors during the last twenty years. Eight of these responded favorably, 3 remained stationary and in 5 there was aggravation of the disease.

The technique of irradiation has gone through several changes. At the present time medium penetrating roentgen rays (25 cm. spark gap and 6 to 8 mm. Al filter) are used with moderate doses at intervals which depend on the response of the lesion to the radiation. In a few instances penetrating roentgen rays (40 cm. spark gap, 0.5 mm zn and 0.2 mm. Al) were used.

The amelioration was chiefly in the sensory disturbances and to a somewhat less extent in the atrophic and vasomotor changes. Not infrequently the muscular weakness and the paretic phenomenon also improved but the muscular atrophy was only rarely modified.

In none of the cases was there a permanent cure.

It is essential that the apparently normal tissues around the involved area be included within the field of irradiation and that the treatment be carried out systematically for a longer period of time.—*T. Leucutia.*

Diacicov, Mihail, Munteanu, V. I., and St. Gavrilescu. Considera tiuni asupra a doua cazuri de tuberculoza miliară iriană vindecate prin radioterapie. (Consideration of two cases of miliary tuberculosis of the iris cured by radiotherapy.) *Cluj. med.*, Oct., 1930, *11*, 496–498.

The authors, after briefly considering the literature on the roentgen therapy of tuberculosis of the iris, describe in detail 2 of their own cases which responded favorably. The technique of the irradiation was as follows: 150 kv., 2 ma., Coolidge tube, 1 mm. Al as filter, 23 cm. skin target distance, 3/5 s.u.d., the dose being administered in three sittings of 1/5 s.u.d. at one to two day intervals, or in case of a more pronounced reaction, at four days' intervals. The treatment was repeated within three to four weeks, a total of two to four series having been given. It is recommended that the irradiation be administered directly on the eyeball (the eyelids being spread apart by a speculum) and that the tube be brought to incandescence before starting the treatment so as to insure a uniform radiation.

In both instances an entire disappearance of the lesion was obtained. Contrary to Rollet and Colrat who maintain that roentgen therapy is of value only in the miliary forms of tuberculosis of the iris, the authors obtained a good result also in one case of the conglomerate type. Likewise they noticed a decrease of the intraocular tension and therefore are of the opinion that tuberculosis of the iris if complicated with ocular hypertension does not form a contraindication to roentgen therapy.—*T. Leucutia.*

Alonso, Justo M., and Oreggia, Juan C. Cancer de la bouche et du pharynx. (Cancer of the mouth and pharynx.) *Rev. sud-am. de méd. et de chir.*, Dec., 1930, *1*, 1266–1267.

The authors have treated a rather large number of carcinomas of the mouth and pharynx, the distribution being as follows: 36 of the tongue, 18 of the margin of the mouth, 23 of the palate, 6 of the gums, 5 of the cheek, 19 of the pharynx, and 33 of the tonsil.

Roentgen therapy constituted the chief method employed. Only temporary improvements were obtained.—*T. Leucutia.*

Keynes, Geoffrey. Radiological treatment of carcinoma of the breast. *Brit. J. Radiol.* June, 1930, *3*, 279–281.

The author gives favorable observations in the treatment of primary carcinomas of the breast which were regarded as inoperable by the surgeons.

He mentions several extreme inoperable cases which responded to radium therapy. The radium was applied via puncture wounds to the actual area of disease both in the breast and in the axillae, above the clavicle, the parasternal glands and in the costocorocoid region.

From his observations he feels that there is a distinct advantage in radium treatment of breast cancer. He does not believe roentgen rays produce as favorable results and do damage the normal tissues more.

The factors involving the application of radium were not given.—*K. K. Alexander.*

Schmitz, Henry. The five-year end-results in carcinoma of the breast. *Radiology*, 1929, *13*, 392–397.

A method has been outlined whereby the clinical grouping of breast cancers may be determined; such grouping is considered an absolute necessity in the prognosis and treatment. The results of treatment show that a carcinoma characterized by fixation, whether it is primary or recurrent, offers a bad prognosis for any method of treatment.

The five-year good end-results in 107 cases of

primary breast cancers were 27.10 per cent and in 143 recurrent cancers 16.85 per cent. The total five-year salvage in 250 cases was 53 cases, or 21.21 per cent.

Attention is drawn to the fact that radiation after operation should not be given until complete healing from the operation has occurred. An operation after a preceding radiation treatment should not be performed until from eight to ten weeks after such treatment. The tumor should show regression, i.e., have been really converted into a freely movable and limited carcinoma. The tissues of the chest wall will recover from the effects of the irradiations within this time and surgical eradication now will be followed by union of first intention.—*J. D. Camp.*

Weatherwax, J. L., and Robb, Charles. Determination of radiation values in lung tissue with variable qualities of radiation. *Radiology*, April, 1930, *14*, 401–409.

In the use of high voltage roentgen therapy the question often arises in the minds of radiologists as to the depth dose of radiation given to lung tissue. Studies by the authors of the effect of the reduced density of lung tissue, with air cavities, on the absorption and scattering of radiation are reported in detail.

The authors' conclusions are that a collapsed lung reduces the measured radiation beneath 2 cm. of water and 3 cm. of lung tissue to a value below the radiation measured through 5 cm. of water, because there is less scattering in the lung tissue. The measured radiation beneath 2 cm. of water and 6, 8 and 13 cm. respectively of inflated lung tissue is greater than the measurements of radiation at the same levels in water alone, because there is less radiation being absorbed. The reduction of scattered radiation caused by the lung being filled with air is more than offset by the decreased stopping power of inflated lung tissue. The isodose charts showing the relative intensity percentages in a water phantom are not high enough for lung tissue. The greatest thickness of inflated lung, 13 cm., approximates the average thickness of male and female through the third costal cartilage, according to Desjardins' anatomical charts of the average patient. The total thickness of the average male through this cross-section is 23 cm., and the thickness of the lung is 14.4 cm., while the total thickness of the average female through this cross-section is 22 cm., with a lung thickness at the greatest dimension of 14 cm.—*J. D. Camp.*

Donaldson, Malcolm. Radiation therapy in gynecology. *Brit. J. Radiol.*, June, 1930, *3*, 246–258.

The author reviews the methods used in treating carcinoma of the cervix in several of the large Continental clinics and then briefly outlines his own preferred method.

The insertion of needles containing 2 mg. of element using a filtration of 0.5 mm. platinum into and around the growth is the usual procedure. The total dose is 7,200 mg-hr. when from 40-50 mg. have been used.

This dosage is rather severe and may result in an irritating proctitis, cystitis or may completely obliterate the upper part of the vagina. It always heals the disease locally.

In dealing with the metastases two methods are used, namely, deep roentgen radiation and intra-abdominal radium application. These methods have not been used long enough to give comparative results of their efficacy.

The intra-abdominal technique is interesting. The abdomen is opened and an examination made of the aortic and iliac glands and the pelvic organs. The needles with the same amount of radium and filtration as mentioned above are inserted into the uterus. They are placed from 1–1.5 cm. apart starting from one sacroiliac synchondrosis to the corresponding point on the opposite side. In addition to this, needles are placed in front of the broad ligaments to irradiate the obturator glands. The abdomen is sewn up completely and the radium left in situ for seven days. At the end of this time a second laparotomy is done and the radium removed.

In irregular hemorrhages at the menopause the author advises the intrauterine application of radium of 50 mg. for 72 hours to be used.

If the condition is menorrhagia alone roentgen rays are used.

In the case of fibroids the authors lays down the following axioms: If the patient is over forty, if the mass of fibroids is not larger than a man's fist, if there is no evidence of inflammatory condition of the appendages, then radium or roentgen radiation is the right treatment.—*F. K. Alexander.*

McEuen, H. B. Report of six cases of malignant melanoma treated with x-radiation,

with two cases cured for over five years. *Radiology*, June, 1930, *14*, 587–590.

Surgery of malignant melanoma should be discontinued, as surgery alone gives a mortality of 100 per cent. Roentgen radiation is the treatment of choice and must be given in very radical dosage, with an attempt at giving the maximum dose within as few days as possible.

If the lesion is in the skin, radiation from a tube excited by 120 kv. is recommended, with probable filtration of 0.5 mm. Al, to prevent marked skin damage from the excessive dose. If the lesion is at a depth below the skin, as in the submaxillary case reported, radiation had best be given from a tube excited at from 200 to 220 kv., with Cu and Al filtration, the maximum dose to be given just under one that would cause permanent damage to the surrounding tissues, that is, a dose approximating 130 per cent S.E.D., administered through a number of ports of entry.—*J. D. Camp.*

Bonanno, A. M. La flora batterica nei carcinomi dell'utero sottoposti a radiumterapia. (The bacterial flora in carcinomata of the uterus after treatment with radium.) *Radiol. med.*, July, 1930, *17*, 809–832.

Having studied the bacterial flora in 20 cases of carcinoma of the uterus the author concludes that it is very variable; staphylococci, saccharomyces and bacteria of the colon type were found most frequently. Streptococci were found in 7 cases.

Radium treatment frequently not only decreases suppuration but also changes the bacterial flora. Biological experiments made with bacteria cultivated before and after the application of radium showed that in some cases the hemolytic and proteolytic properties of the bacteria were increased by the radium treatment. The author found that tumors of the cervix with a rich bacterial flora from suppuration do not respond to radium therapy as sensitively as those which have few bacteria. In the 20 cases he treated, even the ones with streptococci, radium therapy never caused septic local or general complications.—*Audrey G. Morgan.*

Sievert, Rolf M. Die γ-Strahlungsintensität an der Oberfläche und in der nächsten Umgebung von Radiumnadeln. (The intensity of gamma radiation at the surface of and immediately around radium needles.) *Acta radiol.*, Aug. 15, 1930, *11*, 249–301.

This article gives the calculations for the distribution of intensity of radiation at the surface of and immediately around radium preparations, particularly radium needles for intubation. The measurements were made with needles of three different diameters (external diameter 1.5, 2.0 and 3 mm.) and six lengths (0.5, 1.0, 1.5, 2.0, 3.0 and 5.0 cm.), the cylindrical wall of the needles being platinum 0.5 mm. thick. The author used a formula given in a former work (*Acta radiol.*, 1921, *1*, 89). The calculations were made with the maximum and minimum values of the coefficients of absorption involved-radium sulphate, platinum and tissues. The results show that the intensity values of different types of needles are practically unchanged by errors in the absorption coefficients. By means of a graphic method of integration it has been proved that the intensity of radiation at the surface of radium preparations of 1 cm. in length and 2.5 mm. outer diameter may be computed as if the radium were concentrated in the axis of the preparation provided an accuracy of within not more than 5 per cent is required.

Starting with the gamma intensities at the surface of the preparation, relative values have been found from which it is possible to determine the radiation time which will give the same dose at the needle surface for different types of needles. As the intensities at the surface are very high on account of secondary beta radiation from the external layers of the preparations, the suggestion is made that a maximum time of treatment might be determined for these surface intensities and for the different types of needles which must not be exceeded.

The results of the calculations are collected in a number of tables and diagrams, from which data in regard to the intensity in any given case in practice may be obtained. Among other things the distribution of intensity in different types of needles all placed in one plane have been investigated and the corresponding curves plotted. The values obtained are only to a certain extent comparable with each other because of the qualitative differences at different distances from the radium needle, caused partly by secondary beta radiation. At the end of the paper, formulas, diagrams and tables are given for determining the intensity of radiation on the surface and in the immediate vicinity of radium preparations.—*Audrey G. Morgan.*

Ullmann, H. J. A new lead preparation for the treatment of cancer. *Radiology*, 1929, *13*, 494-495.

A new lead compound, lead-calcium phosphate, is described. It is less toxic to the blood than preparations previously used, the primary effect on patients being an increase in both hemoglobin and the red count and not producing anemia in any of the 8 patients on whom it had been used. The effect on carcinomata is apparently as great as that with other lead preparations. One case is reported.—*J. D. Camp.*

Bolaffio, Michael. Der gegenwärtige Stand der gynäkologischen Radiotherapie. (The present status of gynecological radiotherapy.) *Strahlentherapie*, 1930, *36*, 201–236.

The functional gynecological diseases that have been treated by roentgen irradiation are abnormal hemorrhage, defective menstruation, dysmenorrhea and sterility, climacteric symptoms and genital pruritus. Excessive hemorrhage can be treated either by roentgen rays or radium and either temporary or permanent amenorrhea may be brought about. Permanent amenorrhea can be brought about in climacteric and preclimacteric conditions with 28 per cent of an erythema dose, which in younger women only causes temporary amenorrhea. Thirty per cent of an erythema dose only causes amenorrhea for a few months in young individuals; it is used chiefly for very anemic patients. Regulation of juvenile hemorrhage can also be brought about by 600 mg-hr. radium and temporary sterilization with about 1000 mg-hr. But dosage is more uncertain than with roentgen rays. The hypophysis, thymus, thyroid and spleen have been irradiated in genital hemorrhage. The author in some cases of hyperthyroidism with hypermenorrhea has controlled hemorrhage with $\frac{1}{3}$ of an erythema dose applied to the thyroid. But the results are not any more to be depended on than those of irradiation of the hypophysis, and castration cannot be brought about by irradiation of the hypophysis, though amenorrhea has been produced by it for eight months and hemorrhage regulated. Irradiation of the spleen often shows temporary but rarely permanent results. It acts like a nonspecific protein body therapy by destruction of lymphocytes.

The so-called stimulant irradiation of the ovaries to improve ovarian function gives the best results in young patients with disturbances of the menstrual cycle or amenorrhea of not more than three years' duration resulting from them; the results are poorer in pure hypomenorrhea and poorest in tuberculous hypomenorrhea or amenorrhea.

Groedel had good results from irradiation in climacteric symptoms, which he attributed to stimulation of ovarian function, but other authors have attributed the effects to different causes, such as destruction of poorly functionng follicles and irradiation of the suprarenals. Other glands, such as the hypophysis and thyroid, have been blamed for these symptoms and irradiated, and some authors have reported good results. Dellepiane had good results from irradiation of the hypophysis and the author not such good ones from irradiation of the ovaries.

Good results have been reported from the irradiation of genital pruritus. Idiopathic cases with eczema and without atrophy react best. The effect is purely local.

The question of roentgen abortion and injury of the offspring is reviewed, and the author concludes that irradiation during pregnancy is dangerous to the child and should be avoided. Opinion is divided as to the danger in conception soon after irradiation but such a pregnancy should not be interrupted. Late conception after irradiation is free of danger, so that both castration and stimulant irradiation are permissible on strict indications, but should not be undertaken lightly until it is certain that there is no possibility of injury to the fetus.

There is great difference of opinion as to whether operation or irradiation is preferable in myoma. The author advocates radiotherapy and prefers roentgen rays to radium. Subserous pedicled tumors should be operated on, especially when there are signs of torsion or necrosis. Submucous pedicled myomas should also be operated on. If there is a suspicion of sarcoma, the sarcoma dose should be used. If there is a suspicion of carcinoma of the body of the uterus an exploratory curettage should be performed and if it is positive operation is indicated. Calcification does not contraindicate irradiation unless it is extensive. In suppuration roentgen irradiation has a good effect, improves the general condition and creates better conditions for operation. Further contraindications to irradiation are pregnancy, the early puerperium and doubtful differential diagnosis from tumor of

the ovary. There is no definite radium dose for myoma. It depends on the size of the uterus and the age of the patient. The roentgen dose used is that for temporary sterilization.

In tuberculosis of the female genitalia small doses of rays should be used over a long period of time; 1/10 to 1/5 of an erythema dose should be given at intervals of several days. It is perhaps better to operate in easily operable cases. In non-tuberculous inflammations temporary castration is indicated for gonorrheal adnexitis and weak irradiation for non-gonorrheal cases.

Gauss gives as indications for temporary sterilization: gonorrhea and tuberculosis of the adnexa, severe ovarian or myoma hemorrhage in young patients, severe dysmenorrhea and pulmonary tuberculosis. Seitz gives adnexitis of all kinds, pulmonary tuberculosis, myoma in young patients, ovarian hemorrhage, climacteric hemorrhage and menstrual psychoses. The author doubts the indication in pulmonary tuberculosis. He thinks if castration is brought about at all in such cases it should be complete castration.

The question of the radiotherapy of malignant tumors of the female genitalia is discussed and the author concludes that operable cases should be operated on, if necessary with amputation of the vagina. Cleaning out the glands increases the mortality considerably and should not be performed. Four to six weeks before the operation a radium irradiation of 2400 to 3000 mg-hr. should be given and after the operation a fractional roentgen irradiation, a homogeneous irradiation of the pelvis with 600–700 R being given in the course of three weeks. Boundary line cases should first be given a moderate radium dose of 3000 to 4000 mg-hr. After three to four weeks a decision should be made as to whether operation can be performed safely or not. If it cannot the same dose of radium is repeated or a somewhat smaller one given and roentgen irradiation given as in inoperable cases. Inoperable cases that are not cachectic or septic should be irradiated at once, preferably by the combined method: 5000 to 7000 mg-hr. given from the vagina or cervix, either in two irradiations of forty-eight hours with an interval of a week between or continuously for six days or more; then a homogeneous roentgen irradiation of 480–600 R within a few days. The whole treatment should be given if possible within three weeks. The whole or a part of the treatment should not be repeated in less than six months and not after six months unless there is a recurrence.

In the discussion following the article the opinions of a number of authors on these points are given.—*Audrey G. Morgan.*

Samek, Julius. Zur Röntgentherapie der mannlichen Gonorrhae. (Roentgen treatment of male gonorrhea.) *Strahlentherapie*, 1930, *36*, 188–192.

Roentgen irradiation has both a sedative and a therapeutic action in gonorrheal arthritis. In the author's cases the pain stopped within twenty-four hours in some cases, and was greatly improved in others. Roentgen treatment alone is enough for cure in some cases, in others combined roentgen and diathermy treatment is used to prevent ankylosis. In arthritis the author uses 150 kv. and 20 to 25 per cent of a skin erythema dose, with a filter of 0.5 mm. zinc, and 1 mm. aluminium. In large joints he irradiates first from one side, and then the other. Two or 3 such doses with intervals of five to seven days are enough to produce a good effect even in old cases. Ankylosis, of course, cannot be cured.

The effects of irradiation are very good in gonorrheal prostatitis. The acute forms, of course, are helped the most. Where only the prostatic glands are involved the nodules are absorbed in a few days, or rupture in the urethra. In parenchymatous prostatitis with inflammation of all of the prostatic tissue, there are three stages. In the first there is hyperemia, congestion and edema, in the second beginning abscess formation and in the third developed abscess. The most important symptom is very painful dysuria. One irradiation often cures the severe general symptoms, and saves the patient from the necessity for further catheterization. Even when abscess formation has begun absorption can be brought about in most cases. If abscess has already developed it must be opened, but roentgen treatment prevents paraprostatic phlegmon and sepsis. Irradiation is given through the perineum and symphysis. About 20 per cent of a skin erythema dose is given to each field, with a filter of 0.5 mn. zinc and 1 mm. aluminum. This technique is also used in catarrhal and suppurative spermatocystitis. Roentgen irradiation is not indicated in chronic prostatitis with sexual neurasthenia. Diathermia is the treatment of choice in these cases.

Roentgen treatment is not particularly effective in acute epididymitis and deferentitis. About the only effect is the sedative action, and there is some danger in irradiating these sensitive organs, though the author has never seen azoospermia in an irradiated case. Follicular and cavernous infiltrations which follow inflammation of Littré's glands respond very well to roentgen treatment. The same is true of inflammations of Tyson's and Cowper's glands, which should be irradiated through the perineum.

In acute gonorrheal urethritis the maximum stage of the process is brought on sooner, but the treatment does not have a real curative action. It is more vaulable in chronic gonorrheal urethritis. About 50 per cent of a skin erythema dose should be applied to the infiltrations which are causing the stricture. After a few days there is an acute exacerbation of the process, with increase of the catarrhal symptoms and reappearance of gonococci in the discharge. The real therapeutic action does not begin until after some two or three weeks. Hard infiltrations are less amenable to treatment than soft ones, and require larger doses. Small doses of roentgen rays may be used for purpose of provocation. They do not have any direct effect on gonococci.

Roentgen treatment of gonorrhea is a treatment for inflammation, the mechanism of which is not thoroughly understood, but the effect is certainly due to general immunizing processes, rather than to local ones.—*Audrey G. Morgan.*

Ganzoni, M., and Widmer, H. Weitere Erfahrungen über den Röntgenabort. (Further experience with roentgen abortion.) *Strahlentherapie*, 1930, *36*, 510–515.

Since their previous work on roentgen abortion the authors have had 39 more cases. They were successful in provoking spontaneous roentgen abortion in 36 of the 39 cases. One case is excluded because forty-nine days after the treatment the patient was curetted elsewhere; the fetus was dead so spontaneous abortion would have occurred in the course of time. One case was a failure. The patient was a woman of twenty-three with pulmonary tuberculosis. Her last period was on June 5, 1925. On Sept. 8 her uterus was the size of a child's head. An irradiation of 265 R was given. Abortion did not take place. On March 2 a living boy was born. A dried and somewhat macerated fetus was born with the placenta. The authors think this failure was due to the twin pregnancy. The dead fetus had acted as a screen to protect the other one. Since then they have irradiated from two fields, one in front and one behind in order to get a uniform distribution of the irradiation throughout the uterus. And they now consider the minimum dose for roentgen abortion 300 R. In one case laparotomy was performed on the ninety-second day after irradiation as it was assumed that the pregnancy was continuing. But a macerated fetus was found and a great increase of the amniotic fluid. In 3 other cases the intervals between the irradiation and the spontaneous abortion were unusually long—155, 180 and 152 days. Although these were advanced cases in the third to fourth month, the course of the abortions after these long intervals was very easy. There was hardly any pain or hemorrhage and only a serohemorrhagic secretion for three or four days. In one case the authors had begun to think that they had irradiated a myoma instead of a pregnancy as the uterus grew smaller each month. This patient was surprised by the abortion while working in the field and was able to work again that same day and the next. In one case the abortion hemorrhage persisted for thirty-five days. In this case there was evidently a retention of parts of the ovum though it had apparently all been delivered. This patient was unable to work for fourteen days. There were no complications in the other cases. The authors believe the method will find a permanent place in medicine. It will require further experience to determine the exact indications but the technique seems to be settled.—*Audrey G. Morgan.*

Miescher, G. Carcinomtherapie mit superponierter (verzettleten) Röntgenbestrahlungen. (Carcinoma therapy with superimposed (fractional) roentgen irradiation.) *Strahlentherapie*, 1930, *36*, 434–471.

Leading roentgenologists, particularly Regaud and his school, have shown that the time factor is very important in the treatment of carcinoma. They have shown that the irradiation should not all be given in the short space of a few hours but should be spread over a period of ten to fourteen days. Radium therapy has proved superior to roentgen therapy in some difficult conditions partly because the time factor has not been considered sufficiently and massive doses of roentgen rays have been given at one time. The first attempt by Cout-

ard to extend the roentgen irradiation over weeks with daily small doses, the fractional or superimposed method of irradiation, gave some very remarkable results.

Studies of the effects of fractionating made on the rabbit's ear showed that with a partial dose of 400 R the tolerance dose of the skin, measured by epilation effect and the late findings and compared with a large dose given all at once, increased distinctly even with a three hour interval. With a twenty-four hour interval the tolerance increased to 2½ to three fold what it was with the single large dose. But with further increase of the interval the increase of tolerance is relatively slight. With an interval of seven days the proportion is 1:4.

The author's experience with the fractional method in 26 cases showed that the human skin also bears large doses over large fields when the treatment is extended over two to three weeks. With a daily partial dose of 200 to 240 R, total doses of 4000 R and more could be given without the late injuries seen by the previous method. Some of his cases were treated as long as two years ago.

The acute reaction began on an average on the sixteenth day and had run its course by the forty-eighth day. Frequently there are more or less extensive erosions. Histologically the course of the reaction in the epidermis is the same as with a single large dose. But in the cutis there are not the degenerative changes in the cells, either in the acute reaction or the late findings, that there are with a single large dose. This indicates that the fractional method has the same effect on the epidermis but spares the connective tissue.

Some of the author's cases were very severe and showed that good results can be obtained with the fractional method even in severe cases. Seven cases of basal cell carcinoma (carcinoma terebrans) were all cured and so far have remained free of recurrence. Among 9 extensive cancers with horny pearls there were 4 cures and 5 failures. The other cases were 4 of carcinoma of the breast, one of carcinoma of the larynx, one of carcinoma of the parotid, one of malignant goiter, 2 of melanoma and one of polymorphous celled carcinoma of bone. All of these cases are clinically free of tumor at the site of irradiation. One case of carcinoma of the hypopharynx was improved but not cured.

In the treatment of skin carcinoma a single intensive treatment is still indicated in cases in which the carcinoma is small enough so that it is not necessary to irradiate a field more than 5–6 cm. in diameter. In these cases the results of intensive irradiation are very good. But for the more extensive and deeper forms the fractional method is better because it spares the tissues more.

Experience with the fractional method so far indicates that it approximates radium therapy in biological and therapeutic action and may replace it in many fields. The material treated by it so far is too small to permit of definite judgment as to its value and the amount of risk in its use is not yet known.—*Audrey G. Morgan.*

Herendeen, Ralph E. Changes in primary and metastatic bone tumors following various doses of roentgen ray. *Radiology*, 1929, *13*, 326–337.

Herendeen states that the response of primary bone tumors to irradiation is governed by the same general rules followed in selecting the amount of irradiation in the treatment of other groups of tumors. Of all the factors to be considered, none is of more importance than the age of the patient, but equally so are the degree of malignancy, rate of growth, size, location, origin and tendency to produce or destroy bone. Biopsy only occasionally supplies knowledge regarding bone tumors which may not be obtained through other procedures, and the hazards of dissemination of tumor cells and infection must be considered. The repair process following irradiation on the tumor cells may be reduced to a minimum.

Primary bone tumors are classified in order of sensitivity as follows: (1) endothelial myeloma or Ewing's tumor, (2) giant-cell tumor, (3) multiple myeloma, (4) osteogenic sarcoma of the destructive type, (5) osteogenic sarcoma of the mixed or destructive and productive type, and (6) osteogenic sarcoma of the sclerosing bone-producing type.

In general, carcinomas require much larger doses than sarcomas. The response of metastatic tumors from mammary cancer as compared with the response of other carcinomatous metastasis to bones is more prompt and indicates a sensitivity seldom demonstrated in carcinomatous metastasis from other glands. Of all the destructive types of carcinomatous metastasis to bones, it appears that hypernephroma is one of the most resistant to irradiation.

Metastases to bone from carcinoma of the bladder are also comparatively resistant to radiation. In metastasis from carcinoma of the prostate numerous diffuse dense sclerotic or osteoplastic areas are seen, and the only effect obtained from irradiation has been in some instances relief from aching and pain. The response to irradiation in invasion of bone and metastasis from carcinoma of the cervix is, as a rule, disappointing, and the same may be said regarding carcinoma of the mouth, tongue and lip.

The majority of cases of endothelial myeloma or Ewing's tumor occur in children. The changes seen in the film are described as a slight decrease in bone density, very slight widening of the medullary canal, slight changes in the periosteum and thinning of the cortex, and involvement in the case of long bones of a large portion of the shaft, frequently from one-third to two-thirds of its entire length. These tumors are sensitive to small doses of radium or roentgen rays, but in order to prevent recurrence, extension or metastasis heavy doses should be given. In the treatment of giant-cell tumors the author seldom gives a dose even approaching a definite erythema.

The technique used is as follows: Roentgen therapy is commonly applied with the so-called low voltage apparatus and technique, 125 kv. (peak), 4 ma., 4 mm. aluminum, a 10- or 12-inch target-skin distance, depending on the case, and 6 or 12 minutes' exposure.

The author believes that the roentgen treatment of giant-cell tumors produces results in general superior to those secured by surgery. He states that if the surgeon persists in the curettage of giant-cell tumors in spite of the evidence accumulated of the advantages of the roentgen ray, his chances for success in the curettage of giant-cell tumors of the head of the tibia are quite definitely less than at the lower end of the femur. He warns against the use of heavy doses in the roentgen treatment of giant-cell tumors. In his experience the cases of giant-cell tumors which had become malignant had been treated by curettage, and the radium buried in some to control the recurrences and the external radiation employed in others were more or less ineffectual.—*J. D. Camp.*

Gouin, J., and Bienvenue, A. Traitement par la radiothérapie fonctionnelle sympathique des prurits vulvaires. (Treatment by functional sympathetic radiotherapy of vulvar pruritus.) *Bull. et mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 428–431.

The authors give one single roentgen treatment over the principal splanchnic in vulvar pruritus due to ovarian disorders. The dose is the same as applied for menstrual disturbances (3 to 4 H, 7° B, 12 cm. spark gap, 2 to 4 mm. Al). The best time for irradiation is eight to ten days before the appearance of the menstrual period.—*T. Leucutia.*

Gouin, J., and Bienvenue, A. Traitement par la radiothérapie fonctionnelle sympathique des prurits diabétiques et des diabétides (influence sur la glycosurie). (Treatment by functional sympathetic radiotherapy of diabetic and diabetoid pruritus (influence on glycosuria).) *Bull. et. mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 431–433.

Two cases of diabetic pruritus in which good results were obtained by irradiation of the principal splanchnic with the technique employed for menstrual disorders (see above abstract) are briefly described. In the first, one single treatment and in the second, three treatments led to a permanent amelioration of the pruritus. —*L. Leucutia.*

v. Kéméri, Dezsö. Ueber Gefahrenquellen bei der dermatologischen Röntgentherapie. (Sources of danger in dermatological roentgen therapy.) *Strahlentherapie*, Sept. 27, 1930, *38*, 187–195.

Leaving out of account errors due to carelessness, the author says that as much as 120 per cent greater dose may be given than was intended. He describes his experience with the roentgen apparatus in use at the Budapest Clinic for skin and venereal diseases from the beginning of 1929. After working with it for some time he found that at times instead of temporary epilation, permanent epilation was brought about and that 30–70 per cent overdosage had been given though the work was done carefully. The machine then worked properly for awhile but again after some time he found that doses of 100 per cent or more greater than those intended were being given. After careful study he found that this was due to an electrostatic charge of the milliammeter. This seemed to be caused by atmospheric conditions. He found with Lambrecht's hair hygrometer that with the hygrometer over 40° and a room

temperature of 15°–20° C. this phenomenon did not occur. But with the indicator of the hygrometer below 40 after one or two hours there was a difference in dosage of as high as 120 per cent. The reason such differences are not reported more frequently probably is that they were partly due to special local conditions. Their laboratory is very dry and very much exposed to the sun. The apparatus is so constructed that it is not shut off between treatments but works continuously often for four or five hours. For this reason the machine may readily take on a high electrostatic charge as there is no opportunity for discharge between the individual treatments.—*Audrey G. Morgan.*

Jaguttis, P. Ergebnisse der Strahlentherapie bei Thyreotoxicose. (Results of radiotherapy in thyrotoxicosis.) *Strahlentherapie*, Nov. 8, 1930, *38*, 557–574.

The author reports his experience in the treatment of thyrotoxicosis by irradiation for 3½ years from 1925 to 1928. He used a Siemens oil inductor, 2.5 ma., 0.08 Å, corresponding to 153.75 kv., filter 0.5 mm. copper and 2 mm. aluminum; focus-skin distance 23 cm. Two thyroid and one thymus fields were irradiated with about 50 per cent of a skin unit dose, or 279 r to a field. A series of 5 to 6 irradiations was given and repeated in eight to twelve weeks. Basal metabolism was determined with a Knipping apparatus.

In about three-fourths of the cases (76.7 per cent) there was a distinct improvement. There were only 7.28 per cent complete cures, which is less than reported in most statistics, but there is no definite objective measurement for cure. Complete physiological cure is hardly possible in an endocrine disease. A comparison of the remaining symptoms in irradiated and operated cases shows that they are about the same. On dividing the cases into severe, moderately severe and mild it is found that the results were best in the severe cases and among these, best in the ones injured by iodin. The more severely the thyroid is injured morphologically and functionally, the better the effect of the rays. It is possible that better results could be attained by adapting the technique and quantity and quality of the rays to the functional condition of the thyroid. It might also be improved by irradiating other endocrine glands as well as the thyroid, particularly the hypophysis —*Audrey G. Morgan.*

Trout, Hugh h., and Peterson, C. H. Cancer of the breast; use of radium and roentgen therapy in conjunction with the radical operation. *J. Am. M. Ass.*, Nov. 1, 1930, *95*, 1307–1310.

The experience of the authors in the use of postoperative irradiation of breast cancers is so good as to warrant its use routinely, there being as high as 30 per cent of five-year cures. Radium tubes with silver and copper filtration were placed in the operative field and under the edges of the wound. In recent years high voltage roentgen therapy was added. No delay in healing of the wound was experienced. Questionnaires answered by 130 radiologists showed that 91 per cent of them believed postoperative irradiation beneficial, while of 138 surgeons, 89 per cent had the same opinion.—*E. W. Hall.*

Radu, E., and Ackerman, S. La radiothérapie dans le traitement de la coqueluche. (Radiotherapy in the treatment of whooping cough.) *J. de radiol. et d'électrol.*, Oct., 1930, *14*, 559–560.

The authors observed two cures of whooping cough following roentgen examination of the chest. Later a larger number of patients has been systematically treated by roentgen therapy with very satisfactory results. The following technique was used: two series of irradiations at seven to eight days intervals, with 5 h, 3 mm. Al, 120 to 130 kv., 4 ma., 60 cm. skin target distance, one area on the chest anteriorly and one area posteriorly, the central ray being directed towards the fifth or sixth dorsal vertebra. Immediately following the treatment there was, as a rule, a temporary increase in the attacks, lasting for a period of several days. Then the spells gradually grew milder and farther apart, and within three to four weeks there was complete cure.

Five rather unusual cases are briefly described. Irradiation in these was started during the third or fourth week of the disease, after all other therapeutic methods had failed.

The conclusion is reached that roentgen therapy forms a very valuable therapeutic agent in the treatment of whooping cough. The effect probably is through the intermediary of the sympathetic nervous system.—*T. Leucutia.*

Asti, Mario Luigi. Osservazioni sulle misure in radiumterapia di superficie. (Measurement of radium therapy at the surface.) *Radiol. med.*, Sept., 1930, *17*, 1065–1083.

The problem of dosimetry in surface radium therapy deserves as much attention as that of measurement in roentgen therapy. But in most places they are still using the irrational and incorrect designations of "millicuries-destroyed" and "milligram-hours." The French school of Proust was the first to have adopted an ionomicrometric unit, the Dominici unit, which is of great value if it is interpreted judiciously. But this unit has never been clearly defined, even by those who introduced it. The author calls attention to the points that are most apt to give rise to confusion. To obviate these causes of error he proposes the following definition: "The dose given in 10 hours by a spherical ionization chamber with a lumen of 1 c.c., with aluminum walls 1 mm. in thickness, placed in such a way as to have its center 26.2 mm. from the middle point of the axis of a tube containing 10 mg. radium. The tube used should have an internal chamber 16 mm. long and filtering walls of platinum or gold equivalent to 2 mm. platinum. The axis of the tube must be normal in the direction in which the distance from the center of the chamber is measured."

The author then describes the best technique for establishing this unit, reporting the results of experimental work by which he proposes to study the capacity of water for the diffusion of gamma rays; from this work he comes to the following conclusions: (*a*) The standardization of model apparatus to be used for surface radium therapy may be accomplished either in their air or at the surface of water; (*b*) but the amount of transmission must always be investigated with water phantoms, the volume of which is as nearly as possible that of the volume of tissue to be irradiated.—*Audrey G. Morgan.*

Pack, George T., and Craver, Lloyd F. Radiation therapy of polycythemia vera. *Am. J. M. Sc.*, Nov., 1930, *180*, 609–617.

The authors report 4 cases of erythremia with splenomegaly and they state that this disease can be properly treated by irradiation. The treatment should be directed toward the bone marrow rather than the spleen. The hyperplastic bone marrow in this disease is radiosensitive. In this type of disease the symptoms of plethora are relieved, the general health is improved, and life is prolonged, by the use of roentgen rays and radium, but these measures are not capable of preventing the usual fatal termination of the disease.—*E. P. Pendergrass.*

Burgheim, F. Zur Röntgentherapie der Agranulocytose. (Roentgen therapy of agranulocytosis.) *Strahlentherapie*, Sept. 27, 1930, *38*, 152–156.

As the picture of agranulocytosis becomes better known it is seen more frequently. It is a sudden, very severe, febrile general disease with necroses of the mucous membranes, particularly of the mouth and tonsils with extreme leucopenia and almost complete disappearance of the granular leucocytes, with normal erythrocyte, hemoglobin and platelet values.

The author has treated 43 cases of agranulocytosis with roentgen irradiation to stimulate the defective bone marrow function. He has found that the condition may be made worse by large doses but that very good results are obtained with doses of 5 per cent of a skin unit dose, or 30 r per field. This is an irradiation of 175 kv., 5 ma., filtered through 0.6 mm. copper and given over four large fields on the lower extremities with a focus-skin distance of 30 cm.; the next day or the day after, the upper limbs are irradiated and if another treatment is necessary the other large bones, such as the shoulder blades, sternum, and ilium. Sometimes the irradiation of the arms or legs is repeated.

The number of cures was small, only about 17 per cent, but many of the patients came for treatment in practically a moribund condition and died in a few hours. As the disease is hopeless without roentgen treatment even 17 per cent of cures is a great advance.

It has been urged that the effect may not be due to stimulation of the bone marrow but to a general action and that the doses are too small to stimulate the bone marrow. But irradiation of other parts of the body, such as the ovaries and testicles did not have any effect and irradiation of normal individuals with the same doses caused a marked rise of leucocytes, sometimes within two hours.—*Audrey G. Morgan.*

Schlanger, Pablo, and de Schlanger, Enriquetta W. Contribution à la radiothérapie des lymphomes malins primitifs. (Contribution to the roentgen therapy of primary malignant lymphomas.) *Rev. sud.-am. de méd. et de chir.*, Feb., 1931, *2*, 141–153.

The authors discuss the value of roentgen therapy in Hodgkin's disease and lymphosarcoma by citing 6 personal observations which are described in detail and illustrated with photographs and roentgenograms.

I. Hodgkin's disease is divided into (1) acute and (2) chronic forms. The acute form and the terminal stage of the chronic form present the same clinical aspect; both are practically uninfluenced by radiation. In the early stages of the chronic form, roentgen therapy often leads to very marked improvement with prolongation of life and occasionally to permanent cure. Hence an early diagnosis is of paramount importance.

II. Lymphosarcoma is divided on the basis of the histologic appearance into (1) the fusiform cell and (2) the round cell type. Only this latter is considered in the present article. It is the authors' contention that the small round cell lymphosarcoma produces metastases only to the lymphatic system when originating from the parenchyma of the lymph node, and to the lymphatic system and other viscera as well when originating from the free lymphatic tissue. All small round cell lymphosarcomas are exceedingly sensitive to roentgen rays.

The method of irradiation applied by the authors in both Hodgkin's disease and lymphosarcoma was the protracted fractional with the following technique: 170 kv. max., 5 ma., 30 cm. skin target distance, 0.3 to 0.5 mm. Cu, 1 H consisting of 1 to 1½ min. exposure.—*T. Leucutia.*

Hammerschlag, Sigfrid, and Knospe, Heinz. Strahlenbehandlung bei myeloischer Leukämie. (Irradiation in myeloid leukemia.) *Strahlentherapie*, Sept. 2, 1930, *37*, 693–695.

A woman, aged thirty-five, came to the hospital on May 16, 1928, with a diagnosis of tumor of the ovary; she had fever and had been in bed some weeks. Blood examination showed myeloid leukemia. Extirpation of the spleen was at first thought of but on account of the patient's bad condition and the enormous enlargement of the spleen it was given up for roentgen irradiation. One-third of a skin unit dose was given on the surface with a neo-intensive apparatus, 190 kv., 2 ma., filter 0.5 zinc and 1.0 aluminum, field 10×15 cm., focus-skin distance 40 cm. There was immediate improvement in the general condition and blood picture and the patient was discharged and told to return at intervals for examination. She did not come back for a year. She had been in good condition until a dentist extracted five teeth in April, 1929, when she had uncontrollable hemorrhage. In May she came back to the hospital with a recurrence of the leukemia and was again give ⅓ of a skin unit dose. She again improved but this time the improvement did not last so long. The irradiation had to be repeated twice but each time the same dose had a good effect on the blood picture. The last irradiation was given on March 24, 1930. Permanent cure is hardly to be expected in this case but the patient reacts well to small doses. If they lose their effect a series of irradiations could be given, which is the usual way of treating this disease. But the results of single irradiations have been so good so far that that plan has been continued.

Ordinarily splenic tumor should not be confused with ovarian tumor. It should be possible to differentiate between the two kinds of tumor by careful vaginal examination and the blood picture.—*Audrey G. Morgan.*

Huet, J.-A., and Sobel, A. Indictions et résultats de la castration ovarienne temporaire par les rayons X. (Indications and results of temporary roentgen castration.) *Bull. et mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 414–417.

There are three indications for temporary castration: (1) local, (2) general, (3) social.

(1) The local indications consist of persistent hyper- and polymenorrhea without infection of the adnexa. (2) The general indications are formed especially by heart lesions and tuberculosis. (3) The social indications are debatable. In certain states of America, especially in California, sterilization is produced for human betterment. In this respect the recent work of Gosney and Popenoe is very instructive.

The technique is as follows: 25 cm. spark gap, 6 mm. Al, 2.5 ma., 2 anterior and 2 posterior ports of entry, 12×12 cm. field, 1000 r per portal. Theoretically, 35 per cent of a skin erythema dose will produce permanent, and 15 to 20 per cent temporary castration. In practice it is best to proceed on the basis of clinical experience, 500 r per portal being repeated until the appearance of the first flashes and immediately after the disappearance of the regular menstrual period. The castration lasts in the majority of instances for a period of eight to eighteen months.

Three cases in which a normal gynecologic condition resulted following temporary castration are briefly described.—*T. Leucutia.*

Huet, J. A., and Sobel, A. Technique et indications de l'avortement thérapeutique par les rayons X. (Technique and indications of therapeutic abortion by roentgen rays.) *Bull. et mém. Soc. de radiol. méd. de France*, Dec., 1930, *18*, 417–422.

In case of surgical contraindications, the authors perform abortion by the roentgen method. The expulsion of the dead fetus follows within twenty-two to twenty-six days after the irradiation. In the second half of the pregnancy occasionally a premature fetus which will live only for a short time is delivered.

The technique is as follows: 25 cm. spark gap, 6 mm. Al, 2.5 ma., 5 H per field of entry, 2 suprapubic ports of entry with cross-fire for the body of the uterus. Occasionally an additional irradiation over the pituitary or an injection of hormovarine is given on the twenty-first day. Three cases in which a successful roentgen abortion was obtained are briefly described.—*T. Leucutia.*

Uebel, Paul. Über die Therapie der Myome und hemorrhagischen Metropathien an der Würzberger Universitats-Frauenklinik 1923–1928. (Treatment of myomas and hemorrhagic metropathy at the Würzburg University Gynecological Clinic 1923 to 1928.) *Strahlentherapie*, Nov. 8, 1930, *38*, 438–472.

The author reports the results of treatment of 597 cases of myoma and 451 of hemorrhagic metropathy at the Würzburg Gynecological Clinic from 1923 to 1928. Since July, 1923, they have used irradiation in the majority of cases. Permanent roentgen amenorrhea can be brought about by a dose of 34 per cent of a skin unit dose, measured in the deep tissues, or about 275 R. But sometimes not even this much is necessary; under particularly favorable circumstances permanent amenorrhea has been brought about by 21 per cent of a skin unit dose, or 180 R, while temporary amenorrhea requires on an average 20 per cent of a skin unit dose, or about 160 R. When radium is used about 3,000 mg-hr. is the dose for permanent amenorrhea and 1,500 mg-hr. for temporary amenorrhea. For private patients the maximum dose of 34 per cent of a skin unit dose is given for permanent amenorrhea, or 3,000 mg-hr. radium. In cases irradiated for sarcoma, the so-called sarcoma dose was used. It was formerly 60 to 70 per cent of a skin unit dose in the deep tissues or 4,000–5,000 mg-hr. radium inside the uterus but it has recently been increased to 100 per cent of a skin erythema dose, or 830 R and about 7,000 mg-hr. When the combined method was used about equal parts of roentgen and radium irradiation was given.

The average time required for irradiation is much less than for operation. The average time for irradiated cases was nine days as compared with nineteen days for uncomplicated surgical cases and twenty-three days for complicated ones. The patients are able to go to work much sooner after irradiation also. Operation shows a much higher mortality and postoperative morbidity than irradiation. The author concludes therefore that the indications for irradiation should be extended in myoma and hemorrhagic metropathies at the expense of those for surgical treatment.—*Audrey G. Morgan.*

Béclère, Antoine. Uterussarkom und Röntgentherapie. (Sarcoma of the uterus and roentgen therapy.) *Strahlentherapie*, Sept. 27, 1930, *38*, 113–122.

The author describes a case of his own cured temporarily by roentgen irradiation, and from this and a general discussion of the subject concludes that roentgen therapy is to be advised after operation for uterine sarcoma as a prophylactic measure against recurrence. Roentgen irradiation is without doubt indicated as a therapeutic and particularly as a palliative measure in all inoperable cases, in all cases in which operation is contraindicated or refused by the patient, in all cases of recurrence and in all cases of metastasis at any site.—*Audrey G. Morgan.*

Polano, O. Diagnose und Therapie eines Falles von Hydrops tubae profluens auf salpingographischer Grundlage. (Diagnosis and treatment of a case of hydrops tubae profluens by means of salpingography.) *Strahlentherapie*, Sept. 2, 1930, *37*, 619–622.

The patient was a woman of thirty-eight. Abortion was performed because of uncontrollable vomiting with a loss of weight of 1 kilogram a day. As she also had a psychoneurosis, vaginal total extirpation of the uterus was performed and the isthmus of the tubes sutured into the vaginal wound. She was discharged well in eighteen days. After a year she returned saying that for several months she had had a copious discharge with intense pain in the abdomen and back and recently with fever. Exami-

nation showed a resistance sensitive to pressure in the vault of the vagina on the right side. This was assumed to be a gravity abscess and puncture of Douglas' pouch gave a little turbid exudate. The next day a discharge of dark fluid secretion from the vagina began and lasted four days, after which the patient was discharged. A year later she returned complaining of a copious discharge and examination showed a fistula opening in the vagina in the midline about 2.5 cm. from the point where the right tube was sutured into the wall. Iodipin was injected into the fistula and a roentgen picture taken, opaque catheters being inserted to show the ureters also. The contrast mass injected through the fistula was entirely independent of the ureters; it proved to be the right tube, dilated with a hydrops profluens. The left tube was normal. Histological examination of the extirpated right tube showed that the epithelium was normal. The hydrops had evidently been caused by closure of the ampulla as a result of a descending appendicitis. The fistula had developed at the site of the puncture a year before. There must have been an adhesion between the tube and the vault of the vagina at this place following the puncture.—*Audrey G. Morgan.*

Seitz, L. Die Röntgenreizbestrahlung der subakuten und chronischen Entzündungen der weiblichen Genitalorgane. (Roentgen stimulant irradiation of subacute and chronic inflammation of the female genitalia.) *Strahlentherapie*, Sept. 2, 1930, *37*, 595–602.

The author reports his experience in irradiating 380 cases of inflammation of the female sexual organs with a stimulant dose of rays. One large field on the abdomen 20×24 cm. was irradiated with 180 kv. filtered through 1 mm. copper and 1 mm. aluminum. The skin dose was 15 to 20 per cent of a skin unit dose and the dose that reached the deep tissues of the pelvis was only 4–6 per cent of a skin unit dose. This is too small an amount to injure the ovaries.

He concludes from his experience that in acute inflammations of gonorrheal origin this irradiation should not be used at all or only with great caution. There is no danger in its use in acute forms of parametritis; in these cases the irradiation generally brings about more rapid absorption or more rapid abscess formation. The chief field of usefulness of roentgen stimulant irradiation is in subacute and chronic diseases of the adnexa and parametritis. Both in pure gonorrheal diseases of the tubes and ones that were probably gonorrheal, though this could not be definitely demonstrated, roentgen irradiation was useful in about $\frac{3}{4}$ of the cases and a valuable supplement to the usual treatment. Parametritis was favorably affected in almost 100 per cent of the cases.

In order to judge definitely of the therapeutic effect not only should the subjective and objective findings be noted but the leucocytes should be counted and the rapidity of sedimentation determined. The effectiveness of the treatment is shown particularly well by these methods in septic forms of diseases of the adnexa and in parametritis.—*Audrey G. Morgan.*

Eymer, H. Weitere Erfahrungen mit der Röntgentherapie der Adnextuberkulose. (Further experience with the roentgen therapy of tuberculosis of the adnexa.) *Strahlentherapie*, Sept. 2, 1930, *37*, 603–608.

The author reports 14 cases of tuberculosis of the adnexa treated by roentgen irradiation at the Innsbruck Clinic in recent years. The diagnosis was made from the history and the general, pulmonary and genital findings. The cases were not operated on and tubercle bacilli demonstrated. Only cases were treated in which the genital tuberculosis was the most prominent feature. It would be useless to give local treatment for the genital tuberculosis if there were active pulmonary, intestinal or urinary tuberculosis.

The patients were from fifteen to forty-four years of age. Only 7 of them had had full-term children and only one of them one abortion. In 8 of the cases there was a distinct history of tuberculosis.

One large field on the abdomen was irradiated with a dose less than the castration dose two to six times with intervals of from a few days to several weeks. In 12 of the 14 cases the local findings were greatly improved by the irradiation. In tumors of the adnexa the tumor rarely disappears entirely under any form of treatment, to say nothing of restoration of function. One of the women was unimproved and one died of tuberculosis of the intestine. The 12 that were improved were relieved of their subjective symptoms and most of them were able to go to work again. There was a rapid fall of fever, improvement of appetite and gain of strength.

The nature of the action of the rays on genital

tuberculosis is not very well understood. Apparently small amounts of rays, less than the temporary castration dose, have the best effect, so it cannot be a bactericidal action. The absorption of the tuberculous granulation tissue and the substitution of connective tissue proliferation for it, is probably caused by substances originating from the destruction of leucocytes. As these women with tuberculosis of the adnexa are practically always sterile injury of the ova is of no importance.—*Audrey G. Morgan.*

Albrecht, Hans. Die temporäre Röntgenamenorrhoe zur Behandlung der endometrioiden Tumoren des Ovariums und Peritoneums. (Temporary roentgen amenorrhea in the treatment of endometrioid tumors of the ovary and peritoneum.) *Strahlentherapie*, Aug. 9, 1930, *37*, 584–589.

Until recently the treatment of endometrioid tumors of the ovary and peritoneum has been purely surgical. The fact that tarry cysts and other endometrioid structures recede after ovarian function stops suggested that they might be successfully treated by roentgen irradiation. So far the method has been used chiefly in endometriosis of the bladder and rectovaginal septum which is not accessible to surgical treatment; with surgical treatment too there is danger of recurrence as long as ovarian function persists. Stöckel and Zondek therefore advise roentgen treatment as the method of choice in the treatment of endometriosis of the bladder and rectovaginal septum, and for young women Stöckel proposes temporary roentgen sterilization.

As roentgen castration had proved so successful for endometriosis of the bladder and rectovaginal septum the author thought it might also be successful for advanced severe cases of bilateral tarry cyst of the ovaries in which operative castration cannot be avoided on surgical treatment. He describes 6 such cases of severe bilateral tarry cyst combined with retrouterine adenomyosis in which he used temporary roentgen amenorrhea with complete success, both as to subjective and objective symptoms. He therefore thinks this the treatment of choice and that surgery should be used only in unilateral hematomas or ones in which conservative operation can be performed and capacity for conception preserved.—*Audrey G. Morgan.*

Heyman, James. Ein erfolgreich röntgenbehandelter Fall von Endometriosis rectovaginalis. (A case of rectovaginal endometriosis treated successfully with roentgen rays.) *Strahlentherapie*, Aug. 9, 1930, *37*, 590–594.

Two years ago the author had an opportunity to treat a case of endometriosis, or more properly speaking, rectovaginal adenomyositis or retrocervical adenofibrosis. He treated it successfully with roentgen irradiation. He used two abdominal and one back field and irradiated one field each day for three successive days. The focus-skin distance for the abdominal fields was 30 cm. and for the back field 40 cm. The filter was 0.5 mm. copper. A high tension apparatus with condensors and a Coolidge tube were used; constant tube tension 145 or 165 kv., current 3 or 6 ma. Percentage deep dose at 10 cm. depth 25 per cent. He gave 7 series of treatments in the course of three months with a total dosage of 1/10 skin unit dose to each field. After the last treatment the patient had no more pain and the tumor decreased slowly in size. Some months later the author palpated a resistance to the left of the uterus and gave another irradiation of 1/6 skin unit dose on the same fields; the infiltration disappeared and did not return. The patient has been able to work the two years since the treatment and has menstruated, but only irregularly. Of course it is possible that there may be a recurrence, but he believes that if watch were kept in such cases and any signs of recurrence promptly treated with irradiation there would be no danger of serious recurrence.

It is hard to give directions as to technique. He believes it is better to give small doses and watch the patient carefully, adapting the further course of treatment to the results than it is to give a so-called castration dose.—*Audrey G. Morgan.*

Kahlstorf, A., and Zuppinger, A. Unsere Erfahrungen mit der protrahiert-fraktionierten Röntgenbestrahlung nach Coutard. (Experience with Coutard's protracted fractional roentgen irradiation.) *Strahlentherapie*, Oct. 18, 1930, *38*, 199–307.

The authors report their experience with protracted fractional roentgen irradiation since April, 1929. Their method followed the principle adopted by Coutard of fractional and prolonged irradiation. They used an irradiation of 168–170 kv., filtered with 0.45 mm. iron chromate, 1 mm. copper and 1 mm. aluminum with a half-value layer of 1.113 mm. copper. The distance (60–100 cm.) was so adjusted that

the desired dose (180 R in their first cases and 150 R in the later ones) was given in one or two hours. The average time of treatment was three to four weeks. The total dose given in this time measured in air, was between 4800 and 7200 R.

The different tumors are classified in groups and cases described, the conditions of irradiation, dosage and course being given. Most of the cases were inoperable, many of them incurable. But in spite of that, among the 52 patients treated 9 have been free of symptoms six to nine months. Seven of these 9 cases were horny pavement cell carcinomas. Of the patients who are free of symptoms 2 show beginning metastases. In most of the other cases there was a palliative effect lasting from one to several months. In carcinomas of the hypopharynx particularly there was almost always a good early effect. When the irradiations were carried out properly the local condition was relieved entirely. In some of the cases there was local recurrence, in others the residual tumor progressed and caused death and in a large percentage of the cases distant metastases developed.

A mucous membrane reaction generally began between the twelfth and fifteenth days and reached its maximum in a few days; it generally lasted ten to fourteen days but showed great variations and healed without leaving any effect. If the mucous membrane reaction lasted longer than three weeks there was danger of later injury. The mucous membrane reaction furnished a standard for determining the necessary and the maximum dose; the danger of late injury is slight if irradiation is stopped as soon as there is a strong mucous membrane reaction. Histologically there is a fibrinous inflammation of the whole mucous membrane.

The skin in the course of three weeks showed slowly increasing redness, then epilation and pigmentation. The skin reaction was dry or moist depending on the size of the dose, the degree of fractioning and the individual sensitiveness to the rays. The dry skin reaction, which consisted of desquamation or a lamellar detachment of the epidermis, healed without leaving a trace in eight to ten days. The moist skin reaction also lasted eight to ten days but varied greatly. If it lasted longer than three weeks it indicated that the skin had been given too heavy a dose. The excoriations healed in all cases and the hair grew again. There were slight skin injuries in 3 cases but only in those in which inflamed skin had been intensely irradiated or another irradiation had been given after the beginning of the true skin reaction. The reaction affected all the layers of the skin.

Retrogression of the tumor began within a few days after the beginning of the treatment. Complete retrogression did not occur unless irradiation was continued until there was a marked mucous membrane reaction. Retrogression of superficial tumors was generally complete a month after the end of treatment. If a residual tumor remained rapid renewed growth began after not less than two months. Metastases may occur early after the first month or two or later, after more than six months. The prognosis of the residual tumor or recurrence is worse the more intense the irradiation has been and the sooner it develops after the close of treatment.

In tumors lying beneath the surface, either primary tumors or metastases, retrogression may begin even during the treatment. It requires a longer time than for superficial tumors and is generally complete in one to two months. Frequently a residual tumor remains and in such cases the authors recommend operation.

The injuries in the authors' cases and in the literature are reviewed and prophylaxis discussed. In addition to temporary changes in the skin and mucous membranes there may be disturbances of secretion of saliva and of taste, transitory edema at the entrance of the larynx and subcutaneous edema. The skin injuries in 3 cases in the form of telangiectases and pigmentation were caused by irradiation of inflamed skin. There was one case of slight induration of the lung. The authors did not see any cases of cardiovascular disturbance such as may occur on irradiation of large fields on the neck. In one case there was edema of the larynx and necrosis of the larynx was found on autopsy; this was caused by continued irradiation in spite of an intense mucous membrane reaction. In another case death was probably due to edema of the larynx; in this case a very large dose had been given. To prevent necrosis of the jaw thorough treatment of the teeth should be given before irradiation.

The success of the treatment depends on proper dosage and careful observation of the skin and mucous membrane reactions.—*Audrey G. Morgan.*

ACTION OF ROENTGEN RAYS AND RADIUM ON THE GASTROINTESTINAL TRACT

EXPERIMENTAL DATA AND CLINICAL RADIOTHERAPY

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SECTION TWO
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(To be Continued in the September, 1931, Issue)

ACTION OF ROENTGEN RAYS AND RADIUM ON THE GASTROINTESTINAL TRACT

INTESTINE

General Considerations

It has long been known that exposure of the entire body of animals is often followed by anorexia, vomiting, and diarrhea. For many years and even now these manifestations are often regarded as part of the systemic reaction to irradiation commonly known as "radiation sickness."[61] It was not until 1912 that the exceptional sensitiveness of the small intestine was convincingly demonstrated, but to this day many radiologists fail to distinguish between radiation sickness and specific reaction of the intestine and attribute the former condition to the action of irradiation on the latter, notwithstanding that, in human beings at least, radiation sickness occurs as frequently when the intestine is wholly excluded from direct exposure as when it is exposed. The only explanation of such confusion is that the systemic (gastrointestinal) disturbance which follows irradiation of the abdomen, especially the upper half, is usually more severe than the reaction to exposure of parts remote from the abdomen. Radiation sickness will be considered elsewhere (page 68).

Many experiments, such as those of HEINEKE and others, in which the entire body of animals was exposed to roentgen rays, have shown that the lymph follicles of the intestine are as sensitive to irradiation as other lymphatic structures, such as the spleen, lymph nodes, thymus and tonsils, and that the effect on these various structures consists chiefly in destruction of the lymphocytes. The action of radiation on the lymph follicles of the intestine is separate and distinct from the effect on the mucosa of the intestine. The data recorded here are confined to a review and analysis of the experimental and clinical evidence bearing on the specific radiosensitiveness of the intestine aside from that of its lymphatic elements.

Animal Experiments

Roentgen Rays. KRAUSE and ZIEGLER (1906–1907) investigated the action of roentgen rays on the internal organs of mice, rats, guinea pigs, rabbits, and dogs, but a large number of systematic studies was made only on mice. To provide suitable controls, the organs of young and adult, unirradiated, animals of the same kind were subjected to comparative histologic examination. Some of the mice, rats, and guinea pigs were irradiated[62] while in broad glass vessels; others were free or suitably fastened. Only the dogs had to be anesthetized. The animals of the first series were divided into groups, and the animals of the several groups were irradiated for two, four, six, eight or ten hours and killed immediately afterward. The entire body of the animals was exposed to roentgen rays and the chief pathologic alterations consisted of destruction of lymphocytes in the spleen, lymph nodes, intestinal lymph follicles and bone marrow. No other changes were found in the intestine after irradiation for two or four hours, but degeneration of the intestinal mucosa was noted in animals exposed for six hours. The animals of the second series were irradiated for six consecutive hours

[61] "Mal des irradiations" of the French, and "Röntgenkater" of the Germans.

[62] The roentgen rays were generated by Müller water-cooled tubes operated by an induction coil of 60 cm. spark-gap, with Walter connection and a three-point Wehnelt interrupter. The quality of the rays varied between 6 and 8 of the Walter scale. The interrupter was so arranged that a spark-gap of 17.5 cm. made the first spark jump at 7.5 amperes with self-induction 4. The apparatus was operated at a potential of 110 volts double concave, and the current in the inductor was about 4 or 5 amperes. The distance between the tubes and the animals was from 20 to 40 cm.

and killed two, four, eight, twenty-four or seventy-two hours afterward. The animal exposed for seventy-two hours died; another irradiated for ten hours died sixty hours later. The intestine showed marked catarrhal inflammation and desquamation of the mucosa; this apparently started in the epithelium overlying the lymph follicles within two hours after exposure.

In another experiment three animals were irradiated for four hours and three for six hours. The intestine of the animals exposed for four hours showed a "marked desquamative catarrh, with an abundance of bacteria, especially in sections rich in follicles." The intestine of one of the animals exposed for six hours showed almost complete disappearance of the epithelium, and large numbers of bacteria in the submucosa and in the lymph channels. The changes in the two other animals were less marked; the changes varied greatly in different parts of the bowel of all the animals. The authors believed that the intestinal alterations were due to invasion of the mucosa by bacteria through destruction of the lymphoid elements of the follicles by the rays.

Regaud, Nogier and Lacassagne (1912) irradiated[63] the abdomen of six healthy bitches. Necropsy was performed on all of the dogs, and the stomach and intestine of four were examined microscopically. The first dog, weighing 13 kg. and about three weeks' pregnant, received 10 Holzknecht units of rather soft roentgen rays[64] over a large portion of the intestine in one hour. The dose at the level of the skin was estimated as $11\frac{1}{2}$ on the Bordier scale. Diarrhea supervened immediately and the dog died in less than thirty-six hours. The uterus was in full abortion, without hemorrhage, but with intense congestion. It contained five embryos measuring from 12 to 13 mm., and separated from the mucosa. There was slight diffuse hemorrhage in the digestive tract, but peritonitis was not present. The intestinal mucosa was red and covered with an abundance of thick, adherent, chocolate-colored mucus.

The second dog, weighing 15 kg., was irradiated over the posterior, pelvic half of the abdomen and received, in one hour and twenty-five minutes, 5 Holzknecht units of soft roentgen rays.[65] The animal soon began to lose appetite and weight and died twenty-two days later. At necropsy, eighteen hours after death, the peritoneum was reddish, but free from exudate, and there was no sign of perforation. Because the dog had eaten chicken bones two days before death and the anorexia began shortly afterward, death was believed to be due to intestinal infection, made possible by the lowered resistance of the intestinal mucosa resulting from irradiation.

The third dog, weighing about 6 kg., received an injection of 0.03 cg. of morphine and approximately 9 Holzknecht units of soft roentgen rays[66] in one hour and ten minutes directed to the region of the stomach, the greater part of the intestine being excluded. The animal did not eat for three days, and its weight fell in ten days to 5.75 kg. Two weeks after the first irradiation the gastric region was again exposed to 9 Holzknecht units under the same conditions as for the first irradiation. Complete anorexia ensued for two days and partial anorexia for a third day. The weight of the animal fell to 5.5 kg. during the next nineteen days, when a third similar dose of roentgen radiation was given to the gastric region. During the next eight months the weight of the animal decreased to 4.5 kg. The entire abdomen was then given 14 Holzknecht units[67] in two hours. This was again followed by anorexia for two days. One hundred and fourteen days later the weight of the dog was 4.3 kg., but its appetite was good and its condition otherwise satisfactory. The entire abdomen again received 22 Holzknecht units[68] in one hour. The dog soon became very ill, stopped eating and had bloody diar-

[63] Müller "rapid" type tube, with water-cooled anticathode. No description of the generating apparatus was given. The dosage was measured by means of pastilles of barium platino-cyanide. The color changes were determined in broad daylight according to the chromoradiometric scale of Bordier and converted into Holzknecht units.

[64] Rays filtered through 2 mm. of aluminium. Focal-skin distance, 25 cm.

[65] Rays filtered through 2 mm. of aluminium. Focal-skin distance, 31 cm.

[66] Rays filtered through 2 mm. of aluminium. Focal-skin distance, 17 cm.

[67] Rays filtered through 3 mm. of aluminium. Focal-skin distance, 28.5 cm.

[68] Rays filtered through 4 mm. of aluminium. Focal-skin distance, 19 cm.

rhea; it grew weaker and succumbed twenty-eight days after the fifth session of irradiation. At necropsy an extraordinary number of Taenia was found in the intestine which did not contain feces or particles of food. The peritoneum was normal. On microscopic examination the midgastric region showed marked atrophy of the glands, which involved particularly the chief cells; this was held responsible for the progressive cachexia.

The fourth dog, weighing 8 kg., received 20 Holzknecht units of soft roentgen rays[69] over the upper part of the abdomen (stomach and part of the intestine) in sixty-five minutes. This was followed by anorexia, bloody diarrhea, progressive emaciation, and death eighty-one days after irradiation. Necropsy revealed perforation and seropurulent peritonitis at the juncture of the anterior two-thirds and posterior third of the small intestine. The small bowel was filled with thick, adherent, mucopurulent material; there was no pus in the large intestine. Microscopic examination of the stomach disclosed polymorphonuclear leucocytic and lymphocytic infiltration of the interglandular connective tissue. The glands of the pyloric region were normal, but those of the fundus showed definite atrophy. The chief cells appeared shrunken and some of the border cells were vacuolated. The epithelium of a portion of the small intestine was desquamated. In some segments the glands of Lieberkühn were partly atrophied, and their epithelium flattened. In other segments marked atrophy of the glands was noted, but they were completely absent from the region surrounding the perforation. Everywhere the interglandular connective tissue showed extensive leucocytic infiltration, which extended into the muscularis.

The fifth dog, weighing 13 kg., received 20 Holzknecht units of soft roentgen rays[70] over the upper part of the abdomen in one hour. This was followed by anorexia, vomiting, bloody diarrhea, and progressive emaciation for six weeks. The condition then improved slightly, but the animal remained cachectic and was killed at the end of three and a half months. At necropsy, the stomach was normal but full of food. In the mucosa of the small intestine, near the juncture of the anterior two-thirds and the lower third, was a rounded ulcer 8 to 10 mm. in diameter, undergoing cicatrization; this was surrounded by a zone of thickening and induration. The small bowel also contained a large number of Taenia. Microscopically there was slight atrophy of the peptic glands, involving especially the chief cells. There was also slight atrophy of the intestinal glands of Lieberkühn and an increase of the interglandular connective tissue, with many migrating cells. The glandular atrophy was particularly marked in the vicinity of the perforation.

The sixth dog, weighing 17 kg., was irradiated[71] twice within fifteen hours over a large portion of the abdomen, three weeks after having given birth to three pups. Forty hours after the first exposure the animal refused food; it was killed at the end of the third day. The stomach contained about 50 c.c. of mucous liquid, and its inner surface was pale but otherwise normal. The intestine contained only sticky mucus and many Taenia. Microscopically the topography of the gastric glands was not disturbed, but the chief cells were shrunken and partially desquamated. About half of the parietal cells were swollen, vacuolated and free from granules. There was abundant evidence of diapedesis. The intestinal epithelium was flatter than normal and was often detached from the stroma of the villi by abundant leucocytic infiltration and by masses of delicate interlacing filaments, probably fibrin. These changes were greatest in a loop of bowel in contact with the abdominal wall. In the glands of Lieberkühn the epithelium was flattened, the cells were shrunken and indistinct, the nuclei swollen and the tubules fragmented; some had completely lost their epithelium. The connective tissue, leucocytic infiltration, and dilatation of the capillaries had increased. The subglandular layer of lymphoid cells was indistinct, and the injured cells were scattered between the glands.

[69] Rays filtered through 4 mm. of aluminium. Focal-skin distance, 18.3 cm.

[70] Rays filtered through 4 mm. of aluminium. Focal-skin distance, 18 cm.

[71] Filter, 0.92 mm. of aluminium; focal-skin distance, 22 cm.; duration of exposure, 65 and 88 minutes respectively; total dose for the two sessions, 70 to 75 Holzknecht units.

From these results Regaud, Nogier and Lacassagne concluded that the superficial epithelium of the gastric mucosa is not particularly sensitive to radiation, but that the epithelium of the fundus is more sensitive than that of the pyloric region; that irradiation may produce acute or chronic lesions according to the dose and the length of survival or observation; that the lesions in the intestine induced by irradiation involve chiefly the villi, the glands of Lieberkühn and the lymphoid and connective tissues of the small bowel; that the epithelium first becomes detached from the villi, the stroma shrunken and the villi finally disappear, and that the glands of Lieberkühn appear most sensitive and can be made to disappear in a few days.

Fromme (1917) conducted many experiments on frogs, axolotls, guinea pigs and mice with roentgen rays. Only the experiments relating to the intestine will be described.

One pregnant guinea pig, in a narrow wooden box with a cover, was exposed (entire body) to unfiltered roentgen rays[72] for ten minutes and, four days later, for fifteen minutes in the morning and again for fifteen minutes in the afternoon of the same day. Spontaneous abortion occurred two days later, a dead, almost mature, fetus 12 cm. long being expelled with placenta. On the following day the mother's respiration became labored and her movements sluggish; she reacted only slightly to stimuli and died. The lungs were pale, the liver and spleen deep red, the small intestine collapsed, and the large bowel well filled, but there was no sign of hemorrhage. The organs were placed in 4 per cent formalin, and sections were stained with hematoxylin and eosin. These showed that the kidneys, suprarenal glands, liver, and capillaries were normal, and that the blood vessels of the spleen were dilated and contained many pigment-bearing and eosinophil cells (colloid or plasma cells). The large intestine contained many large blood pigment cells, and the stroma was full of migratory cells containing hemosiderin. The blood pigment cells lay in a loose, reticular, connective tissue around the glandular epithelium, which was undergoing vacuolar degeneration. In the small intestine secretion of mucus had increased, and hyperplastic, giant epithelial cells with elongated nuclei were present.

A second guinea pig was irradiated[73] for three minutes on each of eight days and died spontaneously five days after the last exposure; its general condition had changed very little. The lungs were pale and contained several small, alveolar hemorrhagic areas, hyperemia and patches of atelectasis, but no infarction. The hemorrhagic areas were characterized by an abundance of fibrin. The spleen, liver, kidneys and testes were dark red, but showed no evidence of hemorrhage; the liver was markedly hyperemic, its central veins engorged, and many erythrocytes were present between the liver cells. Spermatozoa were absent from the testis, but the spermatids were generally abundant and the Sertoli cells were preserved. In the spleen there was evidence of great destruction of lymphocytes, and an abundance of iron pigment. The epithelium of the small intestine was injured and desquamating, and the nuclei were largely destroyed or markedly vacuolated. Large accumulations of blood pigment were noted in the villi along the course of the vessels, and many hemosiderin cells were present in the stroma. The reticular stroma of the large intestine was so full of hemosiderin cells as to give an impression of melanosis.

A white mouse was irradiated[74] one day for fifteen minutes with filtered roentgen rays and for forty-five minutes (without a pause) with unfiltered rays. The animal was decapitated immediately afterward, its organs were hardened in 4 per cent formaldehyde and sections were stained with hematoxylin and eosin. The spleen, liver and kidneys were markedly hy-

[72] The rays were generated in a Müller, boiling-water tube and directed from above downward through the wooden cover of the box and through the back of the animal. The quality of the rays was given as 11 Wehnelt; the other technical conditions were not specified.

[73] The technical conditions were identical with those used in the preceding experiment.

[74] The entire animal was exposed by means of a Müller boiling-water tube; 3 to 3.5 ma.; focal-skin distance 21 cm.; quality of rays, 11 Wehnelt. Other technical factors were not mentioned.

peremic. The nuclei of many of the hepatic cells were in a state of degeneration. The protoplasm of the epithelial cells of the small intestine had undergone vacuolar degeneration.

A second mouse was likewise exposed to unfiltered roentgen radiation[74] for fifty-five minutes. The following day it became apathetic, respiration was slow and difficult, and it died. Hyperemia of the liver, spleen and kidneys was found, but the intestinal epithelium was uninjured. The liver showed many binucleated cells, as if active division had been taking place, and the nuclei of many of the cells had been destroyed. The spleen gave evidence of great destruction of lymphocytes; the capillaries and the supporting tissue were also disorganized, and many erythrocytes had been ingested by phagocytes.

A third and a fourth mice were irradiated,[75] first for ten minutes with filtered roentgen rays and then for twenty minutes with unfiltered rays, in small doses in the course of five days. The animals became dull and apathetic, breathed with difficulty, and died on the last day of exposure. There was hyperemia of all the internal organs. Some of the hepatic cells were binucleated. Great destruction of lymphocytes had occurred in the spleen which presented a washed-out appearance. The epithelial cells of the small intestine were severely injured and their nuclei degenerated.

Fromme concluded that the chief pathologic changes were: hyperemia of the liver with degeneration of nucleus and protoplasm of many of its cells; great destruction of lymphocytes in the spleen, with phagocytosis of erythrocytes and of an extraordinary quantity of pigment, and the appearance of myeloid giant cells; increased coagulability of the blood attributed to the separation of fibrin ferment from disintegrated leucocytes; leucopenia; vacuolar degeneration, with desquamation or disappearance of epithelial cells of the small intestine, hemosiderosis and leucocytic infiltration; aspermatogenesis in the testis, and fatty degeneration of the heart.

Hall and Whipple (1919), in an extensive investigation of the mechanism of roentgen-ray intoxication, exposed the sides of the thorax and abdomen[76] of thirteen dogs to roentgen rays of different quality. Seven dogs were exposed to roentgen rays[77] for 500, 200, 210, 200, 200, 300, and 400 milliampere-minutes, respectively; these doses were equally divided between the four fields and were given at one session, after a preliminary period of from three to six days, during which the animals were usually starved before the metabolic studies were initiated. Three of the animals were anesthetized with chloroform one or two days before irradiation in order to determine the effect irradiation might produce on the liver independent of the changes produced by the chloroform. Two dogs received once in the same manner 500 and 100 milliampere-minutes, respectively, of roentgen radiation.[78] One dog was irradiated twice, with an interval of twenty-five days between the exposures; the first dose was 300 milliampere-minutes of soft roentgen rays,[79] and the second dose was 400 milliampere-minutes of more penetrating radiation.[80] The remaining dog was irradiated three times with an interval of nine days between the first and second irradiations, and of eighty-four days between the second and third irradiations.

After a latent period of from twenty-four to forty-eight hours following each irradiation, clinical manifestations of systemic intoxication developed in all the animals. The manifestations appeared rather suddenly and consisted in vomiting, diarrhea and general depression. Usually the animals lost appetite, but water was taken with avidity. The symptoms of in-

[75] The technical conditions, although not specified, were presumably the same as in the first experiment. The entire body was exposed.

[76] The remainder of the body was presumably protected from the rays, but no specific statement on this point was made. The size of the fields was not stated.

[77] Rays generated at a voltage equivalent to a spark-gap of 9 inches (probably between blunt points) and filtered through 2 mm. of aluminium. Focal-skin distance, 10 inches.

[78] Rays generated at a voltage equivalent to a 6-inch spark-gap.

[79] Rays generated at a voltage equivalent to a 6-inch spark-gap.

[80] Rays generated at a voltage equivalent to a spark-gap of 9 inches (probably between blunt points), and filtered through 2 mm. of aluminium. Focal-skin distance, 10 inches.

toxication increased, reaching a peak on the fourth day after irradiation; death supervened about the same time. A few animals seemed to improve, but succumbed three or four days later with renewal of gastrointestinal symptoms; in these evidence of secondary infection was found. During the latent period between irradiation and the onset of toxic phenomena, the nonprotein and urea nitrogen of the blood increased; Hall and Whipple interpreted this as due to increased breakdown of body protein, but the dogs appeared quite normal during this period.

Macroscopic and microscopic examination of the parenchymatous organs did not disclose constant abnormalities, except in the spleen which was generally smaller and more fibrous; the difference in size was due to a decreased number of lymphocytes. The bone marrow also showed a decrease in cells. The kidneys did not give evidence of nephritis attributable to irradiation; nor were there any recognizable anatomic changes in the epithelium.

The outstanding and constant pathologic alteration concerned the intestinal tract. The stomach was usually normal, but, in the fatal cases, the mucosa of the small intestine was mottled and there were patches of congestion, often most marked in the jejunum. The capillaries and villi in these areas were distinctly engorged. Patches of congestion were sometimes seen in the colon, which was firmly contracted. The small intestine also showed a tendency to spastic contraction; its contents were occasionally tinged with blood. The contents of the colon were sometimes quite dark. The epithelium of some of the crypts was degenerated and surrounded by large clumps of polymorphonuclear leucocytes, which were also present in the mucosa near the basement membrane of the crypts. The tips of the villi appeared immune to such reaction. The rate of autolysis of the intestinal epithelium was greatly increased; sometimes the epithelium was completely autolyzed when the other organs showed only slight postmortem change.

Hall and Whipple regarded the systemic reaction in dogs and the pathologic changes in the intestine after irradiation of the abdomen as akin to the intoxication caused by intestinal obstruction. Consequently, they considered the pathologic changes in the small intestine as the probable cause of the nonspecific systemic reaction which so often followed irradiation.

Denis, Martin and Aldrich (1920) attempted to elucidate the cause of the systemic reaction[81] which often follows exposure of patients to roentgen or radium rays by studying on rabbits the effect of irradiating different regions of the body. For several days before exposure, the animals were fed oats, celery tops and cabbage. Then from 15 to 25 c.c. of blood was withdrawn from the heart of each animal for chemical examination, and, after a recuperative period of from eight to twenty days, each rabbit was irradiated[82] over a single field $4\frac{1}{2}$ inches square corresponding to the anterior portion of the thorax, the upper part of the abdomen, the lower part of the abdomen, or both thighs. The rest of the body was shielded with lead 1/8 inch thick.

The abdomen of one rabbit was given 120 milliampere-minutes, but this was not sufficient to produce a toxic reaction. Later the same rabbit received, as did all the other animals, 200 milliampere-minutes divided into five sessions each lasting four minutes, with an interval of four minutes between sessions. The nonprotein nitrogen, creatinine and creatine of the blood were estimated by the method of Folin and Wu; the fat, by the method of Bloor, and the alkaline reserve, by the method of Van Slyke and Cullen.

The lower part of the abdomen of five rabbits was irradiated as described. In six days the first animal had lost appetite and weight, and the output of urine had diminished; diarrhea developed eight days after exposure and the rabbit was killed. The stomach was filled with food and the intestine was dilated with gas. There were no abnormalities in the stomach, in-

[81] Sometimes called "irradiation sickness," "mal des irradiations," "Röntgenkäter."

[82] Broad-focus Coolidge tube supplied by a Snook interrupterless transformer, operating at a voltage corresponding to a parallel spark-gap between points of 8 inches; filtration, 2.5 mm. of aluminium; focal-skin distance, 8 inches; intensity of current, 10 ma.

testine, liver, kidneys, or spleen. The second animal manifested symptoms of intoxication four days after irradiation, developed diarrhea twelve days after irradiation, and was killed twenty-two days after irradiation; it had lost 505 gm. in weight. The stomach was filled with food, the small intestine was dilated with gas, and the large intestine with liquid feces; a few hyperemic areas were noted. The kidneys, liver and spleen were normal. Microscopic examination of the injected areas in the large intestine revealed complete loss of epithelium and masses of fibrin and leucocytes overlying the denuded submucosa. The third rabbit became ill and refused food about seven days after exposure; diarrhea developed nineteen days after irradiation, and the animal was killed twenty-two days after irradiation. It had lost 344 gm. in weight. There was nothing abnormal in the stomach, intestine, kidneys, liver or spleen. In the fourth rabbit the usual signs of intoxication developed ten days after irradiation, diarrhea developed fourteen days afterward, and the animal was killed twenty-two days after irradiation. It had lost 419 gm. in weight. The only abnormality noted was a few injected areas in the large intestine; these showed complete loss of epithelium on microscopic examination, and the denuded areas of the submucosa were covered with fibrin and leucocytes. Clinically, the fifth rabbit reacted like the four preceding animals.

Examination of the blood showed a rapid fall in the number of leucocytes, with subsequent regeneration. In two of the animals the nonprotein nitrogen was definitely increased and the alkaline reserve decreased; there was a rise in blood fat in one rabbit. The creatinine values remained unchanged. In two other animals there was no increase in the nonprotein nitrogen or fat and no evidence of acidosis. The urine of all the animals was examined frequently, but albumin, casts or acetone bodies were not found. The fifth rabbit gave late evidence of great reduction in the alkaline reserve and of marked retention of phosphates. Albumin, casts and acetone were never found.

The entire thorax and the upper part of the abdomen of one rabbit were irradiated, and the symptoms which appeared subsequently were identical with those in the previous experiment (loss of weight, diarrhea, prostration).

The thorax only of three rabbits was exposed to the same dose of roentgen rays as in the preceding experiments. The first animal showed only a slight loss of weight at first, but later weight increased and the rabbit remained well for forty-six days after exposure. Radiodermatitis in the irradiated region appeared about twenty days after exposure. The second rabbit remained well for twenty-eight days, and its weight increased 140 gm. The third animal remained well throughout the twenty-six-day period of observation, although it lost a few grams in weight. These three rabbits did not present evidence of intoxication, and the nonprotein nitrogen and alkaline reserve were not affected at any time. Both thighs of one rabbit received the same dose of roentgen radiation, but, in spite of radiodermatitis, the animal's health remained excellent during the four weeks that followed irradiation.

In order to determine whether or not there might be any difference in the toxic symptoms produced by irradiating the anterior and the posterior aspects of the abdomen, the anterior median portion of the abdomen of one rabbit and the posterior median portion of the abdomen of another rabbit were exposed to 200 milliampere-minutes of roentgen radiation under the same conditions as in the preceding experiments. The first animal became ill three days later, and diarrhea set in the following day. Blood was withdrawn from the heart on the eighth, twelfth and eighteenth days, and death ensued from hemorrhage resulting from the last puncture. This animal lost 555 gm. in weight. The second rabbit was well for eighteen days after exposure, when it began to lose weight. Severe diarrhea developed on the twentieth day and the animal died about forty-eight hours later. It had lost 605 gm. in weight. The alkaline reserve of both rabbits diminished following irradiation. To combat the possible objection that under-nutrition might have been responsible for the drop in the alkaline reserve, two rabbits were kept for twelve days on a daily ration of 100 gm. of lettuce and water. These two animals also lost weight, but their blood did not give evidence of acidosis.

On the basis of these results, which apparently corroborated those of Hall and Whipple on dogs, Denis, Martin and Aldrich felt that there must be a definite relationship between irradiation and the toxic manifestations which follow it and the lesions in the small intestine which they noted in their experimental animals. However, in some of the experiments in which the reaction was particularly severe there were no intestinal lesions. This inconsistency impelled Denis, Martin and Aldrich to suggest that the intestinal abnormalities described by Hall and Whipple and noted by themselves may have been the result rather than the cause of the systemic intoxication. Attention is called to the fact that the dose of roentgen rays employed was about five times that given to any one part of a human being, except when "cross-firing" is used. The authors suggested that, in spite of the difference between the toxic symptoms manifested by their animals and those manifested by human beings under radiotherapeutic conditions, such symptoms may be due to acidosis.

KELLER (1921) tested the action of irradiation on the intestine of guinea pigs by exposing the abdomen from the level of the xiphoid cartilage to that of the anterior superior spine of the ilium to different doses of roentgen rays. The remainder of the body was shielded from the rays. The two animals of the first group weighed 450 gm. and 435 gm., respectively. One animal received a dose of seven discharges[83] in one hour, and the second, a dose of fourteen discharges in two hours. The first animal was killed forty-eight hours after irradiation and the second died immediately afterward. Polymorphonuclear leucocytosis appeared one hour after exposure of the first animal; this reached a maximum six hours after exposure, after which the polymorphonuclear leucocytes diminished rapidly, dropped to a low level between one and six hours after exposure, and then gradually increased. The total leucocytes fell in the forty-eight hours from 8,100 to 3,000. Nuclear degeneration and beginning disintegration of the lymphocytes in the spleen and lymph follicles of the intestine also were noted, but the integrity of the intestine otherwise was preserved.

Three guinea pigs, weighing 500 gm., 540 gm., and 530 gm., respectively, were irradiated in the same manner. The first animal received fourteen discharges over the abdomen, and the second and third, fifteen discharges in two hours.[84] The first animal became emaciated, lost 170 gm. in weight, and died twenty-three days after irradiation without any sign of intestinal injury. The second developed anorexia on the sixth day, lost 110 gm. in weight and died in a stupor and with subnormal temperature on the seventh day after irradiation. The third animal developed anorexia and diarrhea on the seventh day; the stools contained blood and mucus on the eighth day, and death preceded by subnormal temperature occurred on the ninth day. The weight had diminished to 60 gm. Polymorphonuclear leucocytosis and lymphocytic leucopenia, both increasing to a maximum between five and six hours after exposure, occurred in all three animals. The total number of leucocytes diminished progressively during the period of observation. The eosinophil, mononuclear and mast cells behaved like the lymphocytes. Pathologic changes were not found in the intestine, spleen or other organs of the first guinea pig. The second guinea pig showed only moderate hyperemia of the upper portion of the intestine; slight follicular atrophy of the spleen; submiliary, focal and probably embolic necrosis of the liver, and hemorrhage into some of the alveoli of the lungs. Hyperemia of the intestine, catarrhal inflammation and localized ulceration of the large intestine, with slight ascites, were found in the third guinea pig.

The abdomen of each of four guinea pigs, weighing 300 gm., 360 gm., 450 gm., and 410

[83] The "discharges" refer to divisions on the scale of a Szilard electroscopic iontoquantimeter. The rays were filtered through 10 mm. of aluminium, and the focal-skin distance was 10 cm. for the first animal and 15 cm. for the second. The other technical factors were not mentioned.

[84] For the first animal the rays were filtered through 10 mm. of aluminium; the second and third received twelve discharges of rays filtered through 10 mm. of aluminium and three discharges of unfiltered radiation. The roentgen rays were generated in a Coolidge tube, but the technical conditions were not stated, except that the focal-skin distance was 15 cm. for the first animal and 10 cm. for the second and third.

gm., respectively, was exposed to thirty discharges[85] of roentgen rays; the first two guinea pigs were each irradiated for two hours and five minutes and the last two for two hours and thirty-five minutes. The first guinea pig was killed in forty hours, and the three others died six, six and seven days, respectively, after irradiation. The first two guinea pigs did not manifest any enteric disturbance, but the second lost 60 gm. in weight and fell into coma several hours before death. In the two remaining animals diarrhea developed five and six days, respectively, after exposure, and the temperature fell below normal. The diarrhea became profuse, the weight fell 100 and 70 gm., and death ensued on the sixth and seventh days, respectively, after irradiation. The changes in the blood were the same as those described in the two series preceding. In three of the guinea pigs the leucocytes almost disappeared from the blood. The spleen, lymph nodes, intestinal lymph follicles and bone marrow showed marked nuclear degeneration and destruction of lymphocytes, scattered nuclear débris and phagocytosis. The entire intestinal tract of the three last guinea pigs was distinctly hyperemic, and varying degrees of epithelial degeneration were noted in different parts of the bowel; this ranged from simple catarrhal inflammation to patches of necrosis, which were covered with clumps of bacteria. Leucocytic infiltration was not a prominent feature. The epithelial degeneration in the intestine was apparently unrelated to the changes in the lymph follicles. Cultures of blood from the heart and also of the stools showed an abundance of colon bacilli. Keller assumed that injury of the intestine by the rays allowed the colon bacillus to pass from the bowel into the blood.

The abdomen of one guinea pig, weighing 400 gm., was exposed to thirty discharges in three hours; the abdomen of another guinea pig, weighing 430 gm., was exposed once to seven discharges in one hour, and a second time, forty-seven days later, to thirty discharges in three hours.[86] *Bacillus prodigiosus* was fed to these animals, by enema and through a stomach tube, before irradiation and daily for five days afterward, to determine if the bacteria would migrate into the blood after intestinal injury. Diarrhea developed in the first animal the fifth day following exposure; the diarrhea became profuse on the sixth day, the temperature fell, and death occurred the same day. The weight had decreased 30 gm. The only clinical disturbance noted in the second guinea pig after the first exposure was slight, transient anorexia, but the second exposure was followed by loss of appetite and of 60 gm. in weight; diarrhea and subnormal temperature appeared on the fifth day and these symptoms increased until the animal died on the sixth day. The leucocytes in the blood, spleen, lymph nodes, intestinal lymph follicles and bone marrow of these two guinea pigs went through the same cycle of reaction to irradiation which was described in connection with the animals of the preceding series. The immediate polymorphonuclear leucocytosis and lymphocytic leucopenia reached a maximum about six hours after exposure, and was associated with progressive total leucopenia followed by regeneration. The data submitted show clearly that the degree and duration of such reaction depended on the dose of roentgen rays which each animal received. The pathologic alterations in the intestinal mucosa were the same as in the preceding series. *Bacillus prodigiosus* could not be recovered from the blood or feces.

Keller concluded that the leucocytes, especially the lymphocytes, and the cells of the bone marrow are much more sensitive to irradiation than the intestinal mucosa, but that the intestine may be injured by sufficiently strong doses of roentgen rays.

Warren and Whipple (1922), seeking an explanation of the systemic, nonspecific intoxication which often follows irradiation of human beings, irradiated[87] the thorax of three adult

[85] The "discharges" refer to divisions on the scale of a Szilard electroscopic iontoquantimeter. The roentgen rays were filtered through 2 mm. of aluminium, and the focal-skin distance was 10 to 15 cm. The other technical factors are not given.

[86] The rays used to irradiate the first animal were filtered through 2 mm. of aluminium; the rays used to irradiate the second animal the first time were filtered through 10 mm. of aluminium, and the second time 2 mm. of aluminium; the focal-skin distance throughout was 10 cm.; the other technical factors were not specified.

[87] Medium hard Coolidge tube. Focal-skin distance, 10 inches; size of field, 6½ inches in diameter; the secondary voltage

dogs, the abdomen being shielded by means of lead foil about 2 mm. thick or by lead rubber about 5 mm. thick, and later the abdomen[88] (thorax shielded) of two of these dogs and of another dog. The animals were kept in standard metabolism cages to facilitate the collection of urine. About 1 c.c. of glacial acetic acid was added to the collecting bottles at the beginning of each twenty-four-hour collection to insure the acidity of the urine collected. The dogs were catheterized daily at 10 A.M. The cage collections, cage washings, bladder washings and catheterized urine were mixed and diluted to a unit volume of 2 liters. The total nitrogen was then estimated in duplicate by the Kjeldahl method. About 300 c.c. of warm water was given daily by stomach tube after catheterization. Water was available in the cages at all times. A subcutaneous injection of morphine, 1/4 grain, was given an hour before each irradiation. The first animal was given a dose of 350 milliampere-minutes over the thorax and its condition remained unaffected. Forty-eight days later the abdomen (thorax, head and neck shielded) was exposed to a similar dose. There were no immediate after-effects, but two days later signs of intoxication appeared in the form of diarrhea; this became marked the next day, and the excreta were tarry, mucous and blood-streaked. There was also frequent vomiting. Four days after the abdominal exposure the animal became weak and dull and later was completely prostrated. The stools were frequent and profuse; the pulse was irregular and thready; the temperature rose to 40.2°C., and the respirations were rapid and irregular. The moribund animal was chloroformed.

Immediate necropsy showed normal pleura, heart, lungs, liver, kidneys and peritoneum; a spleen normal in size, but hard and granular in appearance; ecchymoses in the mucosa of the bladder; slightly enlarged mesenteric lymph nodes; a small necrotic mass in the left suprarenal gland; 20 c.c. of bile-stained fluid and some gas in the stomach, and a thick-walled, spastic duodenum containing many large round worms and reddish-black mucus. Beyond a point 2.5 cm. distal to the pylorus the mucosa of the duodenum was dark red and glassy, and there were several longitudinal folds with bright red hemorrhagic crests. Many bright petechiae appeared between these folds. The reaction in the jejunum was less intense; the mucosa was paler and the plicae were less conspicuous. The ileum contained a small amount of reddish-black mucus and a few round worms. The intestinal wall was thin and flaccid, and the intensely hemorrhagic mucosa appeared denuded of most of its villi. Peyer's patches seemed to have lost their villous covering. These changes ended sharply at the ileocecal valve, although a few longitudinal, hemorrhagic folds were found in the colon.

Microscopically, the lungs, heart, liver, pancreas, kidneys, bladder, uterus, and stomach were normal; the mesenteric lymph nodes were slightly hemorrhagic and contained pigment; the spleen was moderately atrophic and also contained pigment. The ova in the ovary were apparently dead. The portion of the duodenum adjoining the pylorus was normal, but just beyond this portion the villi were collapsed and denuded, with remnants of dead epithelium and some regenerating epithelial cells. Certain areas had escaped injury. In the jejunum the epithelium of the villi and crypts had disappeared. A few crypts remained, and the epithelium surrounding them was undergoing regeneration. Large, pale epithelial cells projected into the lumen of the crypts, and the cytoplasm of these cells was finely meshed and eosinophilic. The submucosa was markedly hemorrhagic and some of the blood vessels were plugged with thrombi of fibrin and platelets. The greater portion of the epithelium of the crypts and villi had disappeared from the ileum. The epithelial remnants showed many mitotic figures

varied between 85 and 103 kv., and the spark-gap between sharp points, between 8¾ and 10 inches; filtration of 2 mm. aluminium; intensity of current, 7.5 or 8.0 ma.

[88] The abdomen was taken as below a line passing transversely through the xiphisternum; the thorax as above this line. The thoracic and abdominal portions were subdivided into an upper and a lower half, and each of these halves was irradiated from the lateral and midventral aspects. In this manner the ventral portion of the abdomen or thorax was exposed to the roentgen rays through six different fields, the contiguous edges of which overlapped. Usually the middorsal portion of the thorax or abdomen also was exposed.

and were clumped in small groups. Mucoid degeneration and slight necrosis of the tips of a few villi were the only changes observed in the colon.

The second dog was given an exposure of 300 milliampere-minutes over the abdomen (thorax, head and neck shielded). Diarrhea, vomiting and prostration followed, but the animal recovered. A month later 350 milliampere-minutes was applied over the thorax (abdomen shielded), without effect. Two months after the first exposure of the abdomen, 350 milliampere-minutes was applied over the abdomen. An hour before each irradiation 1/4 grain of morphine had been injected into the animal. The after-effects were the same as in the first dog, and the pathologic changes found at necropsy and on microscopic examination were essentially the same.

The third dog, after a preliminary injection of 1/4 grain of morphine an hour before irradiation, was exposed to 350 milliampere-minutes of roentgen irradiation[89] over the thorax only, without apparent effect. Forty-five days later the same dog was irradiated for 450 milliampere-minutes over the abdomen (thorax, head and neck shielded) and was killed by ether four days later. The intrathoracic organs and structures were found normal; the pathologic changes in the abdominal organs were not described.

The fourth dog also received an injection of 1/4 grain of morphine an hour before it was given 340 milliampere-minutes' irradiation over the abdomen through seven fields, as in the other animals; the thorax and lower part of the pelvis were shielded with lead foil. Symptoms of intoxication (vomiting, diarrhea and prostration) appeared after two days and became severe the following day with much blood in the stools. The dog was comatose when it was killed by ether. Immediate necropsy disclosed normal thoracic viscera and serous surfaces, liver, spleen, suprarenal glands, lymph nodes, kidneys and genitourinary tract. The stomach was filled with blood-streaked mucus, but its pale mucosa was otherwise normal. The pathologic changes in the intestine resembled those observed in the other dogs that had received abdominal irradiation under approximately similar conditions. One dog was given a smaller dose of 300 milliampere-minutes over the abdomen, with the thorax, head and neck shielded. Four days later vomiting and diarrhea developed, but these toxic disturbances disappeared in about ten days and the animal recovered.

In commenting on their results, Warren and Whipple stated that, although after irradiation there was complete disappearance of the red marrow cells from the ribs, only moderate destruction of lymphocytes in the lymph nodes and intestinal follicles, moderate atrophy of the spleen, with shrinkage of malpighian corpuscles, no injurious effect on the corpuscular elements of the circulating blood, or on the lungs, heart and pleura; no change in the liver, pancreas or suprarenal glands and only slight renal alterations, the effect of roentgen rays on these different structures could not have anything to do with the general systemic intoxication so common after irradiation. The gastrointestinal tract, on the contrary was regarded as especially sensitive to roentgen rays, and this was held to apply chiefly to the small intestine, the stomach and colon being comparatively resistant. The rays were held to act with particular force on the epithelium, which undergoes necrosis and disappears. Warren and Whipple, therefore, believed that "the symptoms of intoxication and the final lethal poisoning are due to this injury of the intestinal epithelium."

Warren and Whipple (1922) carried out further studies on the influence of roentgen rays on the abdominal viscera by irradiating[90] each of the four quadrants of the abdomen of five adult mongrel dogs, weighing from 20.5 to 45 pounds. The animals were irradiated only after a fasting period of from two to four days, and 1/4 grain of morphine was given before irradiation.

[89] 117 milliampere-minutes with a current intensity of 7.5 ma. at 103 kv.; 233 milliampere-minutes with a current intensity of 10 ma. at 90 kv. (spark-gap between sharp points, 9 inches); focal-skin distance, 10 inches.

[90] The roentgen rays were generated at voltages ranging from 89 to 97 kv. (probably root-mean-square), corresponding to a parallel spark-gap of approximately 9 inches; the focal-skin distance was 10 inches; the filtration, 2 mm. of aluminium; the current intensity, 8 ma. for the first dog, and 7.5 ma. for the four others; the exact size of the fields was not specified.

The first dog received irradiation to each of the four abdominal quadrants of 480 milliampere-minutes between 3 and 5 P.M., and was killed at 6 P.M. by bleeding under ether anesthesia. Immediate necropsy showed normal viscera, except for the kidneys, the cortex of which revealed a few scars. The intestinal tract was wholly normal. Microscopic examination of all the abdominal organs[91] disclosed arteriosclerosis and dense scars in the kidneys; hyperplasia of the prostate gland; nuclear fragmentation in the center of the follicles of the spleen and mesenteric lymph nodes, and a fuzzy appearance of the nuclei of the epithelium lining the crypts of the duodenum and jejunum; these changes were more readily perceptible in the adjacent lymph nodes.

The second dog was given 450 milliampere-minutes to each abdominal quadrant at 2 P.M., and at 2 P.M. the next day, while still entirely normal, was killed by bleeding under chloroform anesthesia. Immediate necropsy showed all abdominal viscera normal, except the small intestine which was tightly contracted and contained bile-stained fluid. The mucosa of the duodenum and jejunum was thrown into longitudinal folds, the crests of which were speckled with ecchymoses. A few other small ecchymotic patches were scattered through the small intestine. The mucosa was unusually bile-stained, but only moderately congested. On microscopic examination, cellular necrosis and many phagocytes were found in the lymph follicles of the spleen and mesenteric lymph nodes. Definite nuclear changes were observed in the epithelium of the crypts of the small intestine; these nuclei were pale and the chromatin fragmented. Polymorphonuclear leucocytic infiltration also was present. The epithelium covering the villi was normal.

The third animal received 450 milliampere-minutes of irradiation to each abdominal quadrant, the thorax and pelvis being shielded with lead. The dog showed no ill effects until two days later, when it vomited bile-stained mucus and was killed, probably by bleeding under ether anesthesia. The only abnormalities noted on immediate necropsy were: bile-stained mucus in the stomach, the mucosa of which was normal; bile-stained mucus and a little bright red blood in one portion of the small intestine, the mucosa of which was pale generally, but showed scattered ecchymoses; longitudinal folds with pink crests dotted with ecchymoses; a few congested patches in the ileum, and a spastic colon, with normal mucosa. Microscopically, the gastric mucosa was normal; a sharp line separated the normal gastric from the abnormal duodenal mucosa, the crypts of which showed fragmented nuclei, cellular degeneration, and a few wandering cells; there was edema of the submucous tissues; the epithelial covering of the villi was unimpaired. These pathologic changes extended throughout the small intestine. The mucosa of the colon was essentially normal, only occasional crypts presenting degeneration of epithelial cells and invasion by wandering cells.

The fourth dog was given 340 milliampere-minutes to each abdominal quadrant, with the thorax and pelvis shielded. Two days later the animal vomited bile-stained material and the stools were stained with blood. On the third day the dog was weak, the stools contained bright red blood, clots and mucus, and it was killed under ether anesthesia. On immediate necropsy the kidneys showed a few cortical scars, and the pancreas slight fat necrosis. The stomach contained blood-tinged mucus stained with bile, but the mucosa was normal. The small intestine contained a little blood-tinged mucus and was irregularly contracted. The mucosa of the duodenum was glassy, dark red, thin and wrinkled in places; it had lost its velvety appearance. The remainder of the small bowel was mottled; Peyer's patches were made conspicuous by the thinness of the small intestine. These changes began sharply at the pylorus and stopped as sharply at the ileocecal valve. The mucosa of the colon was pale and contained a few ecchymotic areas. There was microscopic evidence of injury to the lymph follicles in the spleen and mesenteric lymph nodes. The ovaries showed degenerating, necrotic ova; there was great destruction of marrow cells in the lumbar vertebrae and much cellu-

[91] Sections fixed in 10 per cent formaldehyde and usually stained with hematoxylin and eosin.

lar débris in large phagocytes. The stomach was essentially normal. Much of the epithelium covering the villi and lining the crypts of the duodenum had disappeared, and many villi appeared as naked, swollen polyps, with dilated capillaries. Some of the crypts were filled with cellular débris. Wandering cells were conspicuous and there was edema of the submucosa. In some portions the mucosa could not be recognized, while in others it was almost normal. The same alterations appeared in the jejunum and ileum.

The fifth animal received 350 milliampere-minutes to each abdominal quadrant, with the thorax and pelvis shielded, and remained well until three days later, when vomiting and diarrhea supervened. On the fourth day the animal became prostrated, the stools contained fresh blood and clots, the temperature fell, and it was killed under anesthesia, ninety hours after irradiation. The pathologic changes were essentially the same as in the other animals.

Warren and Whipple mentioned that irradiation was followed by a slight but constant increase in urinary nitrogen in all the animals. They also stated that "the epithelium of the small intestine is at least as sensitive to the x-rays as are the lymphocytes of the same area. In fact, by a large dose of the x-rays, we can actually destroy all of the epithelium, while many clusters of lymphocytes still remain." From these experiments they concluded that the epithelial injury in the small intestine was the result of irradiation and that such injury was responsible for the progressive and lethal intoxication.

Warren and Whipple (1922) exposed the abdomen of five dogs to from 300 to 480 milliampere-minutes of roentgen rays, and killed the animals under chloroform or ether anesthesia two, twenty-four, forty-eight, seventy-two, and ninety-six hours, respectively, afterward. One set of sections of each organ was immediately fixed in 10 per cent formaldehyde for control. Five sets of sections, each section weighing from 3 to 5 gm., were cut from each organ immediately after death. The sections were placed, while still warm, in a bottle containing about 150 c.c. of warm 0.9 per cent sodium chloride solution previously saturated, while warm, by shaking for an hour with an excess of chloroform. All the bottles were warmed to 37°C., corked, placed in an incubator at 37°C., and the tissues allowed to autolyze. One set of sections was removed after four, eight, ten, twelve and twenty-four hours, respectively, and immediately fixed in 10 per cent formaldehyde. There was no putrefactive odor in the bottles, even after autolysis for twenty-four hours. Organs from three normal unirradiated dogs were treated in the same manner to serve as controls.

The sections[92] were studied with regard to the effect of irradiation on the rapidity of autolysis in vitro, and opinion was based on the intensity of staining of the nuclei, the integrity of cell outline and cell contents, and the complete digestion of the cell itself. Fibroblasts, mature connective tissue cells, endothelial cells and macrophages, muscle tissues, and certain leucocytes were little, if at all, disturbed by the long irradiation. The tissues of both the control and irradiated animals resisted autolysis, and appeared little changed even by autolysis for twenty-four hours at 37°C.

The spleen, liver, pancreas and lymph nodes of the irradiated animals were more rapidly autolyzed than the same organs from the normal control animals; this was most striking within twenty-four hours in dogs killed seventy-two and ninety-six hours, respectively, following a lethal dose of roentgen rays. There was no such change in the kidneys. Abnormal autolysis of the small intestine was apparent even ninety-six hours after exposure, this indicating that the intestinal cells still suffered from the injury inflicted by the rays, even four days after exposure.[93] The increased rate of autolysis of the villi was affected last, while the reverse was true in the normal small intestine of the control animals. The colon showed little change and the stomach no appreciable change in autolysis under similar conditions. Warren

[92] These sections were made from the organs of the dogs used in the preceding experiment. All the histologic material was fixed in 10 per cent formaldehyde and stained by the hematoxylin-eosin method (paraffin sections). About 600 slides were reviewed at least three times as unknown specimens to prevent bias.

[93] The clinical symptoms always reached a crisis on the fourth day.

and Whipple did not attempt to appraise the significance of this disturbance of cell ferments in the intestinal mucosa, but felt that it corroborated the profound functional disturbance of the intestinal epithelium.

Martin and Rogers (1923) tried to ascertain the specific susceptibility of the intestine to roentgen rays by exposing[94] to their action loops of dogs' intestines that had been brought out ten to fourteen days before under ether anesthesia and spread on the abdominal wall so that both the intestine and the skin would receive approximately the same dose. To test the experimental conditions one medium-sized dog[95] was given 200 milliampere-minutes over each flank. Three days later the animal refused food, diarrhea developed, and it was found dead on the morning of the fifth day. Several loops of small intestine were dilated and hyperemic, and the bowel was quite thin in places. The most pronounced lesions were in the duodenum. Tests of the erythema dose for the skin of the dog[96] showed that 75 milliampere-minutes of irradiation produced a definite reaction; it required 150 milliampere-minutes to cause shallow ulceration.

On the basis of these preliminary tests, a loop of ileum 31 cm. long was brought out through a suitable incision in the abdomen of a female dog of medium size, and through an opening 6.5 cm. square in a lead shield, and was given 25 milliampere-minutes of irradiation while spread between two layers of gauze moistened with a warm solution of physiologic sodium chloride. The cutaneous margins of the abdominal incision were in the field of irradiation. Sutures were then placed in the mesentery as markers, the intestine was returned to the abdominal cavity, the incision closed, and the abdomen bandaged. Three weeks later the skin in the irradiated region showed no sign of reaction, and the dog was in excellent health. At necropsy the serous and mucous coats of the irradiated loop appeared normal.

A loop of intestine (lower part of jejunum and upper part of ileum) 44.5 cm. long was similarly brought out from the abdomen of a medium-sized dog and given an irradiation of 75 milliampere-minutes.[97] The animal recovered satisfactorily, except for a stitch abscess. A faint erythema appeared eight days after exposure, and on the twelfth day the skin was deep red. This subsided, and by the twentieth day only alopecia marked the exposed area. The dog remained well and active. It was killed after three weeks, and the irradiated loop of bowel could be distinguished by its abnormally smooth appearance and by hyperemia of the subserous vessels. The most striking change was the shortening of the loop, which measured 15.5 cm. between the markers. The velvety appearance of the mucosa had disappeared, and the inner surface of the intestine was smooth and dark red. The epithelial layer had disappeared from these dark red areas. The limits of injury were sharply defined. There was no evidence of hemorrhage, and the intestinal contents were normal in color.

A loop of small intestine 12.5 cm. long was brought out in the same way from the abdomen of a small dog[98] and was given 100 milliampere-minutes of irradiation. The animal recovered promptly and remained well for three weeks; it was then killed. The irradiated loop of bowel was contracted, hyperemic, smooth, and measured only 6.5 cm. in length. The greater portion of the epithelium had disappeared from the mucosa of the exposed loop and that which remained was necrotic. The submucosa was thickened and infiltrated with leucocytes. The muscle fibers also were vacuolated, but no pathologic changes were found in the blood vessels.

A loop of small intestine 26.5 cm. long was brought out from the abdomen of a large, pregnant bulldog[98] and given 150 milliampere-minutes of irradiation. The upper end of the

[94] The technical conditions were as follows: voltage equivalent to a 5 inch parallel spark-gap between points; sphere-gap indicating 75 peak kv.; intensity of secondary current, 10 ma.; focal-skin distance, 10 inches; size of field, 3½ inches square, with the remainder of the body shielded with lead foil.

[95] Age and weight not stated.

[96] The skin of the dog is approximately three times more resistant to irradiation than the skin of man.

[97] Minimal erythema dose for the dog.

[98] Age and weight not stated.

uterus was within the field of exposure. Erythema over a small portion of the irradiated skin appeared about ten days later, but the animal remained in excellent condition for two weeks, when it was killed. The skin in the exposed region was slightly ulcerated. The irradiated loop of intestine, which measured only 12.5 cm. in length, was recognizable by its smoothness and by hyperemia. The mucosal surface of the loop was smooth and red, and there was no trace of epithelium.

A loop of small intestine 23 cm. long was brought out in the usual manner from the abdomen of a medium-sized dog[99] and given 150 milliampere-minutes of irradiation. The animal remained well for two weeks, but after sixteen days it refused food, began to lose weight and became progressively weaker and very ill; it was killed on the nineteenth day The pathologic changes were the same as in the preceding experiment.

Martin and Rogers believed that all the dogs would have shown more or less deterioration of health, according to the dose of roentgen rays, if they had been observed longer. They added that these experimental results could not be applied directly to human beings because of the unknown difference between the sensitiveness of the intestine of the dog and that of human beings; also that a certain degree of injury to the intestine is compatible with life, but that injury beyond a certain point is likely seriously to disturb health and may cause death.

Warren and Whipple (1923), having determined experimentally that sufficient doses of roentgen rays directed to the intestine cause degeneration and desquamation of the intestinal epithelium, and that the denuded villi and crypts are covered by masses of exudate and bacteria, attempted to ascertain to what extent bacterial invasion from the intestine occurs. The abdomen of five healthy, normal dogs was irradiated,[100] and the animals were killed by bleeding under chloroform anesthesia twenty-four, forty-eight, seventy-two, ninety-six and ninety-six hours, respectively, after exposure. One normal, unirradiated dog was used as a control. The body was washed with lysol and immediately opened with sterile precautions. Small blocks of tissue for culture were taken from the lungs, liver, kidneys and mesenteric lymph nodes. The spleen was not cultured. The blocks of tissue were seared, and small bits from the interior were cultured in 1 per cent glucose broth for twenty-four hours; 25 c.c. of blood from the heart was put into 250 c.c. of 1 per cent glucose and also cultured for twenty-four hours. Enrichment cultures were plated on Endo's medium and plain agar; these enrichments were usually inoculated in beef heart mediums, aerobically and anaerobically. *Bacillus coli* was identified by the usual sugar tests. Smears of the intestinal contents and of the organs were made at the time of necropsy. Smears of the organs were usually negative.

One dog, killed twenty-four hours after abdominal irradiation, did not show qualitative evidence of invasion by organisms other than *Bacillus sporogenes*, cocci and other bacteria usually found in the normal dog. There was histologic evidence of injury to the chromatin of the crypt epithelium of the small intestine, but cellular destruction and symptoms of intoxication were not observed. One dog, killed forty-eight hours after abdominal irradiation, showed disintegration and desquamation of many of the epithelial cells lining the crypts of the small intestine, and only moderate leucocytic infiltration. *Bacillus coli* was cultured from the mesenteric lymph nodes, left lung and right kidney; invasion of the lymph stream was indicated. One dog, killed seventy-two hours after abdominal irradiation, had shown evidence of marked intoxication during life, and great destruction of the epithelial cells lining the intestinal crypts was found at necropsy. *Bacillus coli* was recovered only from the mesenteric lymph nodes. The other organisms were the same as those found in normal animals. Two dogs, killed ninety-six hours after abdominal irradiation, were acutely intoxicated. The intestinal mucosa of both dogs was practically destroyed. *Bacillus sporogenes* was found in all the organs; *Bacillus coli* in the mesenteric lymph nodes and right kidney; *Bacillus wel-*

[99] Age and weight not stated.

[100] The technical details of irradiation were not given. It is probable that these bacteriologic studies were made on dogs included in other communications from the same authors.

chii in the mesenteric lymph nodes, right and left kidney, right lobe of the liver and right lung. In one of these two animals both *Bacillus sporogenes* and *Bacillus coli* were found in blood from the heart, and *Bacillus coli* was also present in the mesenteric lymph nodes, lungs and left lobe of the liver. Cocci were found in the lungs and right kidney. Cultures of the blood from the heart of all the animals remained sterile until the last day of intoxication or until almost the agonal period.

Stained slides of the fixed sections from the lumen of the ileum and colon and between the villi and crypts showed large masses of bacteria, mostly Gram-positive rods. Few bacteria were seen in sections from the duodenum. In the markedly injured sections bacteria were found among the disintegrated epithelial cells and against the denuded basement membrane, but it was not found that organisms had invaded the stroma, even where the villi had collapsed and open capillaries were present. There was no evidence of local bacterial invasion of the intestinal wall at any point. Profuse excretion of fluid was noted throughout the intestinal tract. Warren and Whipple concluded that, in spite of extensive destruction of intestinal epithelium by strong roentgen irradiation of the abdomen, an overwhelming invasion of the tissues, lymph and blood by intestinal bacteria does not occur, and that the intestinal epithelium is not an indispensable barrier against bacteria.

Swan (1924) studied the action of roentgen rays on the isolated and intact small intestine of the rabbit and cat. The roentgen rays were generated in gas tubes, and no attempt was made to filter the rays.[101] "The experiments on the isolated intestine were made with lengths of rabbit's small intestine hung up so as to record longitudinal movements. The fluid was oxygenated Tyrode solution containing a trace of magnesium sulphate, and kept constantly at 37°C. After the intestine had been recording for a time sufficiently long to be sure of its condition, exposure to x-rays was begun. The tone began to rise after about twenty minutes of exposure; the automatic contractions usually remained of about the same degree as before, but the relaxation was less complete." After further irradiation the tonus increased still more and relaxation diminished. No abnormal "interference" was observed between the circular and longitudinal fibers.

"The automatic movements of the intestine in anesthetized cats and rabbits were recorded by a small manometer connected to a loop of intestine enclosed in the abdomen and ligatured at the distal end." The loop of intestine, measuring 8 or 10 cm. in length, and the manometer were filled with liquid paraffin, and the movements of the paraffin in the distal end of the manometer were recorded. This showed both pendulum movements and peristaltic waves. The effect of roentgen rays was to increase the automatic movements, and the tonus also was slightly increased. Similar effects were produced in the cat, but the tonus of the entire intestinal muscle increased. The tonus diminished gradually after cessation of irradiation.

Ceresoli (1924), without describing his experiments,[102] stated that strong roentgen irradiation of the colic and hypogastric regions of rabbits causes high grade hyperglycemia; that the normal glycemic level rises day by day if irradiation is carried out on four consecutive days, but shows inconstant variations afterward. Irradiation of the right side of the abdomen, exclusive of the liver, also causes hyperglycemia, but the blood sugar returns to normal after four hours. Ceresoli believed that the increase in blood sugar was probably due to the influence on the liver of toxic products of cellular degeneration in the intestine or to inhibition of pancreatic function as a direct effect of irradiation.

Ivy, McCarthy and Orndoff (1924) studied the effect on gastric secretion of roentgen irradiation of the thorax and abdomen, with the stomach excluded. Eleven dogs[103] were used

[101] Distance from anticathode to intestine, 7 inches; potential equivalent to a spark-gap of 5½ inches; current passing through the tube, 1.0 ma. Duration of exposure, 40 minutes.

[102] The blood sugar was determined by the macrochemical method of Schaffer and Hartmann.

[103] Age and weight not stated.

for this purpose, and the surgical preparation of the Pavlov pouch, as well as the pre-irradiation and post-irradiation tests of gastric secretion were conducted as in their earlier investigation of the action of direct roentgen irradiation of the stomach. In two animals, 1 mg. of histamine was injected before irradiation, and again during the period of anorexia following irradiation, in order to ascertain if the gastric secretory mechanism itself was involved. Necropsy was performed on all but one of the animals that died. The intestine was examined microscopically.

The left thoracic wall of two dogs with Pavlov pouch was exposed once to roentgen rays[104] for seven minutes. Thirteen or fourteen days later the skin peeled and a shallow ulcer appeared, which persisted for about two months without healing. The irradiation did not cause symptoms and the gastric secretion was not altered during the two months that followed irradiation.

The lower right side of the abdomen of two other dogs was irradiated once[104] for thirty-seven minutes in one dog and thirty minutes in the other. Irradiation was followed by early vomiting, anorexia, and, in one dog, by diarrhea. The gastric secretion of one animal diminished greatly four days after irradiation and none was produced between the fifth and tenth days. Secretory function reappeared and increased slowly with return of appetite.The free hydrochloric acid and the total acidity also diminished, but such chemical variation was not great. Gastric secretion did not form in the Pavlov pouch of the second dog for eleven days after irradiation; it then reappeared and gradually returned to normal by the twentieth day, with return of appetite. The free hydrochloric acid and the total acidity diminished one-third in thirteen days and then slowly returned to normal. In spite of the tendency of the appetite to recover and of the stomach to recover its secretory activity, the animals became emaciated and cachectic, and died twenty-three and fifty days, respectively, after exposure. This decline was accompanied by renewed and progressive anorexia and by fresh depression in gastric secretion.

The entire abdomen of seven dogs was irradiated once[105] from the right side. Four of the animals vomited within half an hour to one hour; two vomited intermittently for two hours, and one for four days. Partial anorexia was also present, and in five of the dogs there was increased secretion of gastric juice during the first two days after exposure to roentgen rays. Partial or complete anorexia, decrease of gastric secretion and anacidity, beginning on the third day and continuing for two or three days, occurred in all the animals. The authors believed that the dogs recovered or died according to their vitality at the time of irradiation. Four dogs died from acute roentgen intoxication in from six to fourteen days. Of the three that recovered from the immediate intoxication, one died from hemorrhage after one month, one from fibrous pancreatitis after two months, and one from experimental intussusception after three months.

The entire abdomen of two dogs was irradiated once[106]; the immediate effects and the influence on gastric secretion were the same as in the preceding group, except that gastric secretion did not increase at any time, and the symptoms of intoxication were mild.

Extensive pathologic changes were found in the intestine of most of the animals. The changes consisted in marked necrosis and autolysis of the epithelium lining the small intestine, and delay in the reaction of the fibroblasts.[107] The histologic changes occurring during the first four days were not observed, but the authors found that the subsequent changes agreed with the observations of Warren and Whipple, except that they could not discern greater destruction of the epithelium of the crypts. "In every case in which the mucosa was not completely sloughed, the crypt epithelium was relatively well preserved, while the villi

[104] Voltage, 110 kv.; focal-skin distance, 30 cm.; filter, 1 mm. aluminium; current, 5 ma.; size of fields, 6 cm. in diameter.

[105] The dose of roentgen rays was: voltage, 200 kv.; focal-skin distance, 50 cm.; filter, 0.75 mm. copper and 1 mm. aluminium; size of field, 11 by 21 cm.; current, 5 ma.; time of exposure, 120 minutes.

[106] The same as in the previous group, except that the time of exposure was reduced to 90 minutes.

[107] For a more detailed description of the gastric changes see page 27.

were either present as naked polypi or obliterated." Goblet cells disappeared from the crypts when the epithelium of the villi was destroyed. When the injury to the villi was less severe the goblet cells appeared more numerous and contained a large amount of mucus. Hyperemia, hemorrhage, and small thrombi could generally be seen. The endothelial cells lining the blood vessels and lymphatics of the intestine were swollen and projected into the lumen. Marked paralysis of the fibroblasts, which underwent hypertrophy but did not show mitotic division or produce collagen, was noted soon after irradiation. Evidence of repair of the injured epithelium was not obtained, even in one dog observed for fifty-four days. The authors believed this may have been due to failure of the connective tissue to react normally. They also found that it was the depth dose and not the surface dose which injured the mucosa of the intestine, and concluded that the mucosa of the intestine is approximately twice as sensitive to roentgen rays as that of the fundus of the stomach. The alterations produced by a dog erythema dose and by a human erythema dose were of the same kind, but differed in the degree of injury. The dose for the dog[108] produced complete sloughing in patches, thus exposing the surface of the intestine as deep as the muscularis mucosae. With the dose for man the villi were obliterated or denuded of epithelium, but complete sloughing did not occur. Extreme atrophy and fibrosis were noted in the pancreas of one dog, in which there was a marked increase in the secretion of gastric juice; the hypersecretion was ascribed to the uncontrolled acid stimulation of the intestine caused by absence of the neutralizing effect of pancreatic juice.

The gastric secretion of most of the animals receiving strong doses increased for one or two days after irradiation of the extragastric portion of the abdomen, but after this the secretory activity diminished more than when the stomach was directly exposed. This secretory depression was attributed chiefly to the anorexia induced by irradiation, and the initial increase in secretory activity either to increased irritability of the intestinal mechanism concerned in gastric secretion or to a reflex spasm of the pylorus from injury or irritation of the intestinal mucosa.

Martin and Rogers (1924) exposed the entire abdomen of five young[109] guinea pigs to roentgen irradiation,[110] the animals being secured to a board with the abdomen uppermost and the head and upper part of the thorax shielded. The doses administered were 200, 152, 72 and 56 milliampere-minutes, respectively. The first three animals became weak, mucous diarrhea developed, and they died at the end of six days. The pig which had received 72 milliampere-minutes, developed diarrhea and cachexia, but lived three weeks, while the pig receiving 56 milliampere-minutes showed no ill effect.

In each of six dogs[111] an isolated loop of small intestine, from 10 to 15 inches long, was exposed to 75 milliampere-minutes of unfiltered roentgen radiation.[112] The loop of intestine was brought out through a small opening in a lead shield, which excluded all other structures. One animal died from peritonitis two days after the operation, and a second dog died from infection after one week. The four other dogs recovered promptly and were normal at the end of three weeks. One of these dogs remained well for thirty-two days, but anorexia developed and it lost weight for fifty-three days, when it was quite emaciated. The irradiated loop of small intestine was resected and the intact bowel anastomosed end-to-end. Large ulcers, with a grayish-green, necrotic surface, were found along one side of the resected loop; the intestinal wall was thickened, but there was no sign of obstruction. The dog died four days later from peritonitis. The second dog of the group of four dogs remained well for thirty-four days, after which anorexia and loss of weight developed; the animal became

[108] Approximately three times greater than the erythema dose for human beings.
[109] About the same age, but the age was not stated.
[110] Technical conditions of irradiation: 9 inch parallel spark-gap; focal-skin distance, 10 inches; filter, 2 mm. aluminium.
[111] Age and weight not specified.
[112] Parallel spark-gap, 5 inches; focal-skin distance, 10 inches; this represents an erythema dose for the skin of the dog.

greatly emaciated during the subsequent fifty-eight days and was found dead on the sixty-fifth day. In the mucosa of the irradiated loop of small intestine were shallow ulcers; the bowel wall was thickened, but there was no evidence of obstruction. In a third dog the same clinical course followed irradiation and the same changes were found at postmortem. The fourth dog remained well for a month after irradiation. Anorexia and emaciation became apparent after forty-one days; these symptoms progressed for fifty-eight days, when improvement was noted; this continued steadily for one hundred and seventeen days; then the animal began to lose weight in spite of a ravenous appetite. This dog was killed one hundred sixty-six days after irradiation, and a moderate quantity of clear, straw-colored fluid was found in the peritoneal cavity. The small intestine above the irradiated loop was dilated to five times normal size. The dilatation stopped abruptly at a markedly indurated strip, which was contracted and measured less than 1 ½ inches in length (the irradiated loop measured 13 inches in length). The intestine below this point appeared normal, and the lower part of the bowel and rectum contained considerable fecal material. When the irradiated loop of intestine was opened it was found stenosed, and the lumen was approximately 3/16 inch in diameter. Small, shallow ulcers were scattered along the mucous membrane for a short distance on each side of the stenosed portion. These pathologic changes were interpreted as an indication that the clinical symptoms (final cachexia in spite of ravenous appetite) were due to interference with absorption or to toxemia secondary to the absorption of toxic material from the lumen of the bowel or from the ulcers in the mucosa.

With the object of clearing the foregoing point, Martin and Rogers exposed isolated loops of small intestine, in three dogs, to 15, 37.5 and 75 milliampere-minutes, respectively, of irradiation.[113] The dogs were not affected, and after a week they were given a half pint of cream in the morning. Three hours later an abdominal incision was made under ether anesthesia. The intestine of the dog which had received 15 milliampere-minutes was normal, and the lymphatics were gorged with fat. The intestine of the two other dogs also appeared normal, but lymphatics could not be discerned in the mesentery of the irradiated loop. This was held to indicate that large doses of roentgen rays directly to the intestine cause inhibition of fat absorption in the exposed region. Martin and Rogers did not believe this could be due to destruction of the intestinal epithelium, because the greater portion of the mucous surface of the intestinal loop, which had received 37.5 milliampere-minutes of irradiation, "showed no gross abnormalities." There were only a few small patches of ulceration, but the remaining epithelial cells had apparently lost the power of absorbing fat. No evidence of intracellular fat could be discerned in frozen sections stained with osmic acid. There was a marked increase in the number of goblet cells. Almost every cell of the mucous membrane was markedly deformed by a huge collection of mucus. This increase in mucus may have been responsible for the loss of absorptive power, but it was not proved, especially since such loss affected only a single loop of the small intestine. However, the rapid death which followed irradiation of the whole abdomen may have been associated with the increase in mucus, which may have interfered with the absorption of water.

Podesta (1925) undertook to test the effect of roentgen rays on the intestine by irradiating the intact abdomen of four dogs. In the first two, both females, weighing 5.8 kg. and 7.5 kg., respectively, the central portion of the abdomen of one dog and the epigastric region of the other were irradiated[114] for seventy minutes and one hundred minutes, respectively. The dog irradiated for seventy minutes was apparently not affected. It was killed three and a half months after irradiation. The intestine appeared to be greatly changed, but, on microscopic examination, both the small and large intestine showed only slight lymphocytic infiltration and variation in the staining quality of the nuclei, with shrivelling and fragmen-

[113] The other technical factors were the same as in the previous experiment.

[114] Size of each of six fields, 8 by 6 cm.; equivalent spark-gap, 34 cm.; filtration, 2 mm. aluminium and 0.2 mm. brass; focal-skin distance, 30 cm.; intensity of current, 3 ma.

tation of the chromatin. The dog irradiated for one hundred minutes was dejected, ate little for nine days, had a slight fever, and passed more feces than usual. Twelve days after the first irradiation the lower right and left portions of the abdomen were irradiated separately for sixty-five minutes. Diarrhea, with bloody stools and fever, followed, and food was refused for three days after the second irradiation. Erythema of the skin of the epigastric region, with desquamation and slight ulceration, appeared eighteen days later and healed in about twenty days, but the skin in this area remained atrophic and bald. When the dog was killed three and a half months after irradiation, its weight had increased 600 gm., and the only perceptible macroscopic change was slight hyperemia under the serosa of some coils of the small intestine. The microscopic appearance of the small and large intestine was the same as that of the first dog, except that the pathologic changes were slightly greater.

The pelvis of a third female dog of moderate size and weighing 6.4 kg. was irradiated[115] in such a way that six beams of roentgen rays converged, three from the front and three from the back. The dog was slightly depressed and did not take food. Anorexia continued for six days, after which the dog recovered its normal appetite. There was no fever at any time, and the weight remained constant for three months, when the animal was killed by puncture of the fourth ventricle. No lesions were found in the small intestine, but there were areas of lymphocytic infiltration in the muscularis mucosae. The microscopic appearance of the small intestine resembled that of the two previous dogs, except that the pathologic changes were even less pronounced.

The lower portion of the abdomen of a fourth dog, which weighed 6.1 kg., was irradiated under the same technical conditions as the previous animal, except that only three converging beams of roentgen rays were directed toward the pelvic region; each field was exposed for seventy minutes. Slight dejection and weakness followed. The dog ate but little, the temperature rose, and diarrhea supervened. Three days later three additional fields over the lower portion of the back were irradiated in the same manner. The animal rapidly became worse, and the liquid feces were mixed with blood; this condition continued for about twenty days. Erythema of the skin corresponding to each field of irradiation then appeared; the erythema proceeded to slight ulceration, which healed in forty days, and the skin over these areas remained atrophic and devoid of hair. The dog recovered its appetite in about a month; nevertheless, it lost 1,300 gm. during the three and a half months following irradiation, at the end of which time it was killed by puncture of the fourth ventricle. General hyperemia of the small intestine and stenotic constrictions were found. Sections through some of these areas of enteritis showed numerous ulcerations, ellipsoid in shape and with the long axis perpendicular to the axis of the bowel. These ulcers corresponded with the stenosed portions, affected chiefly the mucosa and seldom extended into the muscular coat. Elsewhere the mucosa was essentially normal, except for scattered patches of lymphocytic infiltration; pycnosis and fragmentation of nuclei were especially prominent in the basal portion of the mucosa. The submucous coat was thickened and contained many large cells, with broad and ill-stained nuclei, while the outline of other cells was indistinct and the nuclei were broken into fragments. Lymphocytes also infiltrated the muscular coat to some extent, the longitudinal fibers being chiefly affected. A large number of young connective tissue cells was found in one section. The condition of the large intestine was essentially the same as in the other animals.

Ten other animals were irradiated in the same general way, with similar results, but details were not given. Podestà added that some of the irradiated dogs became markedly emaciated, while others, that had received stronger irradiation over a large number of fields, developed severe diarrhea, took no food, and died within from two to five days. Podestà concluded that the erythema dose for the skin of the dog is much greater than for

[115] Size of each of six fields, 8 by 6 cm.; equivalent spark-gap, 34 cm.; filtration, 2 mm. aluminium and 0.2 mm. brass; focal-skin distance, 30 cm.; intensity of current, 3 ma.; time of exposure to each field, 40 minutes.

that of man; that a suberythema dose (dog) produces pathologic changes in the intestinal mucosa; that a dose sufficient to cause erythema or dermatitis in the dog produces more definite alteration in the intestine, and that a suberythema dose to each of several converging fields causes intestinal lesions approximating those caused by an erythema dose to a single field.

Tsuzuki (1926) conducted a series of experiments on rabbits, the entire body of which was exposed to strong doses of roentgen rays generated at relatively high voltage; the technical part of these experiments is described elsewhere (page 9). After death the intestine showed pathologic changes, which varied from mere destruction of lymphocytes in the mucosa and atrophy of the lymph follicles to degeneration and desquamation of the epithelial investment of the bowel. The lymphocytic destruction was perceptible within three hours after exposure; the degenerated and scattered chromatin of these cells later underwent phagocytosis, but extensive lymphoid regeneration also was noted. The epithelial degeneration was greatest in the upper part of the small intestine, apparently starting in the crypts of Lieberkühn, and was associated with moderate lymphocytic infiltration. A tendency to epithelial regeneration was manifested subsequently.

Domagk (1927) carried out an extensive investigation of the action of roentgen rays on the kidney. Heavy doses were directed to the region of one or both kidneys on one or more occasions at relatively short intervals. The field of irradiation often included the spleen, the liver, and a portion of the intestine. The kidneys of most of the animals showed early degeneration of the tubular epithelium, hyperemia, edema and sometimes infarction, often followed by proliferation of connective tissue leading to more or less pronounced sclerotic atrophy. The liver and spleen also showed degenerative changes when within the field of exposure. In some of the animals the part of the intestine in the path of the rays likewise developed degenerative changes. In all of the animals anorexia and loss of weight developed after irradiation and "a large number of them showed symptoms of diarrhea—undoubtedly due to involvement of the intestine in the irradiative injury." Unfortunately, the condition of the bowel of only a few of the animals was described. In these instances, however, the following changes were noted: hemorrhage in the wall and into the lumen of certain portions of the intestine; multiple small hemorrhages in, and erosions of, the mucosa scattered throughout the remainder of the intestinal tract; degeneration of the epithelium, and accumulation of blood-streaked mucus and deposition of fibrin and leucocytes on the denuded surface of the mucosa, and hemorrhage in the muscularis.

Radium. Löhe (1912), impelled by Orth's report of a death attributed to thorium X, undertook experiments on five healthy, adult dogs weighing from 7.05 to 9.45 kg. The thorium X was injected into the vein of the left hind foot. The five animals received on the same day 2,000,000, 1,000,000, 500,000, 250,000, and 100,000 Mache[116] units, respectively. The first dog was killed three days, and the four others died twelve, fifteen, nine and nine days, respectively, after the injection. Moderate hyperemia of the entire large intestine and of parts of the small intestine of the first animal was found. The intestinal changes in the other dogs were more severe; besides general hyperemia of the large intestine, the crest of the folds of mucosa was bright red or dark brown and hemorrhagic. In the small intestine occasional bright red patches of petechial hemorrhage were scattered here and there. The intestinal lymph follicles were greatly swollen. The kidneys showed innumerable, discrete or coalescing, red points in the cortex and medulla. Microscopically, the mucosa and submucosa of the large intestine was hyperemic and contained many hemorrhagic areas. The kidneys also were markedly hyperemic, and erythrocytes were found in the capsular space of some of the glomeruli. Swelling and deficient nuclear staining of the epithelium were noted in some of the convoluted tubules. The pathologic changes varied in extent and degree ac-

[116] The Mache unit is the quantity of radioactive substance without disintegration products, which produces a saturation current of 10^{-3} in a chamber of large dimensions. 1 curie = 2.5 by 10^9 Mache units.

cording to the dose of thorium injected and the time elapsed between the injection and death.

One dog, weighing 1.51 kg., was given two injections of thorium X, each of 250,000 Mache units, with an interval of one week, and died four days after the second injection. The small and large intestines were strewn with petechial hemorrhages, and there was an abundance of coagulated blood in the large bowel. A dense blood clot adhered firmly to the mucosa at the ileocecal valve. In the large intestine the crests of the folds were markedly hemorrhagic. Hemorrhagic areas were also found scattered throughout both kidneys. Microscopic examination confirmed the nature of these changes. One dog, weighing 8.65 kg., was given two injections of thorium X, each of 100,000 Mache units, with an interval of one week, and died ten days after the second injection. Only slight hyperemia of the large intestine was found at necropsy. The animal was emaciated, but the small intestine and kidneys appeared normal.

Mayebo (1913) tried to ascertain experimentally why and how intravenous injection of large doses of thorium X produces hyperemia and hemorrhage in the kidney and intestine, especially the large intestine. For this purpose ten healthy dogs, each weighing about 9 kg., were selected and divided into five groups of two dogs. As a preliminary step each dog was operated on. The intestine was divided just above the ileocecal valve, and the distal end of the small intestine was sutured to an opening in the skin, while the proximal end of the large intestine was likewise sutured to an opening in the skin of the abdomen remote from the first opening. The two dogs of each pair were then injected with the same amount of thorium X at the same time (two to three days after operation), and one dog received colonic irrigations once or twice daily, while the other served as control.

The first two dogs, which had received 500,000 Mache units of thorium X, died three days after the injection. Of the second pair, which had also received an injection of 500,000 Mache units of thorium X, the dog whose colon had been irrigated daily died, and the other was killed, six days after injection. Of the third pair, which had received 570,000 Mache units of thorium X, the animal whose colon had been irrigated daily died, and the other was killed, seven days after injection. The two dogs of the fourth pair each received 200,000 Mache units of thorium X on two successive days and a third injection of 500,000 Mache units four days later. The animal whose colon was irrigated daily died, and the other was killed, three days after the third injection of thorium X. The two dogs of the fifth pair each received 500,000 Mache units of thorium and a second injection of 170,000 Mache units the following day. The animal whose colon was irrigated daily died, and the other was killed, five days after the second injection. Apathy and anorexia supervened the day following the injection of thorium X. Loss of strength was greater and death ensued earlier in the dogs whose colon had been irrigated than in the control animals. At necropsy, neither hyperemia nor hemorrhage was found in any part of the intestine of the control animals, with the exception of the control animal of the first pair, the intestine of which showed, especially in the colon, hyperemia and many bright red and brown petechial hemorrhages. Scattered hemorrhages were also noted in the serosa of the large intestine adjoining the ileocecal valve in the control animal of the third pair, while its companion that was irrigated showed hyperemia and many petechial hemorrhages along the crests of the folds of intestinal mucosa in the ileocecal region. Among the dogs whose colon had been irrigated daily, pronounced hyperemia and numerous hemorrhages were found in the ileocecal region of the dogs of the second and third pairs; the hemorrhages in the intestinal mucosa were very slight.

Mayebo interpreted these results as meaning that, while the dose of thorium X injected played a significant part, the time between the injection and death was still more significant. He proceeded to test this deduction on five healthy dogs weighing from 9 to 10 kg., the first of which received 500,000 Mache units and each of the four others 600,000 Mache units of thorium X intravenously. The three first animals were killed three, five and seven days,

respectively, after injection; the fourth and fifth died thirteen and fifteen days, respectively, after injection. The intestinal mucosa of the first dog showed a moderate accumulation of mucus, but neither hyperemia nor hemorrhages. The mucosa of the small and large intestine of the second dog was covered with thick mucus, and in the large intestine the crests of the folds of mucosa showed numerous fresh petechial hemorrhages. Similar but more numerous petechial areas were noted in the large intestine of the third dog, and also in the small intestine for a distance of 10 cm. above the ileocecal valve. In the fourth dog, discrete and coalescing petechial hemorrhages were scattered throughout the small and large intestine and they often extended into the submucosa. They were especially marked in the lower three-fourths of the large bowel. The mucosa of the bladder also showed such hemorrhagic areas. The intestinal hemorrhages were still more pronounced in the fifth dog, and they were noted also in the stomach, kidneys and bladder.

Mayebo, therefore, concluded that the large intestine is one of the chief pathways for the elimination of thorium, and that the marked effect of this substance on the mucosa of this portion of the intestine is due to the slow movement of its contents and to the longer time allowed for the action of thorium in comparison with the small intestine and kidneys, which suffer less injury from the same dose.

Lazarus-Barlow (1922) exposed the entire body of twenty frogs, twenty-eight rats, fifteen rabbits and nine cats to the gamma rays emitted by 5 gm. of hydrated radium bromide. A detailed description of these experiments will be found elsewhere (page 10). Symptoms were not observed in the majority of animals, but rabbits allowed to survive after exposure for forty-eight hours became somnolent and, in one instance, hemorrhage from the ears occurred. In two animals an initial loss of weight was recovered during the second week after exposure. There was no evidence of diarrhea, but after prolonged exposure there was impaired intestinal action. In the cats symptoms did not appear for one or two days after exposure, but soon or long after this, according to the duration of irradiation, the animal refused food and became somnolent. Mucus sometimes exuded from the mouth or anus and diarrhea occurred in some cases.

After short exposures the epithelium investing the duodenum and lining the tubular glands was swollen and loosened. Desquamation of some of the cells and vesiculation of nuclei were noted. There were no mitotic figures, few goblet cells and little mucus. The stroma was scanty and contained few cells. As the period of survival increased after exposure of moderate duration, degeneration and desquamation advanced rapidly, much nuclear débris was found in the blind ends of the tubules, goblet cells became numerous, and ill-formed masses of chromatin suggesting mitosis were found. The stroma became edematous and contained endothelial, small mononuclear and plasma cells, but no polymorphonuclear leucocytes. Desquamation of the epithelium sometimes led to necrosis of the stroma. Later, these changes became more marked, and the lumen of the intestine contained much desquamated epithelium mixed with mucus, or evidence of improvement was found when the exposure had been moderate. After long exposure entire tracts of mucous membrane underwent mucoid degeneration. Even the stroma became intensely edematous and its connective tissue fibrils became gelatinous or collagenous. Brunner's glands also were ultimately destroyed. Hemorrhages were rarely seen.

The pathologic changes in the jejunum resembled those in the duodenum. After long irradiation or survival they were most pronounced in the rat and rabbit. Mucoid degeneration was always a prominent feature. The condition of the ileum was similar to that of the upper segments of the small intestine, but less intense. Yet pronounced changes were present, even to the point of complete sloughing of the mucosa. The lumen contained much desquamated epithelium and mucus. The tubular glands were converted into bags of mucus, and goblet cells were numerous. The persistent nuclei were vesicular or deeply stained and con-

tracted. Deformed mitotic figures were seen. The stroma was edematous and moderately cellular, and contained some lymphocytes but no polymorphonuclear cells.

Degeneration and desquamation were less marked in the large than in the small intestine, but here also an excessive formation of mucus was present. There was extreme conversion of columnar into goblet cells, both in the investing and tubular epithelium. Most of the tubular glands showed only the outlines of cells with deeply stained, contracted or linear nuclei pressed against the basement membrane or between contiguous cells. Many of the goblet cells were empty and the mucus was in the lumen of the intestine. Only slight desquamation was found. Some isolated cells had become converted into large, oval, deeply stained, homogeneous masses; these, while seen chiefly in the rectum, were also present in the colon and occasionally in the small intestine.

MOTTRAM (1923) exposed six rats continuously to 220 mg. of radium.[117] The animals were killed with gas after exposure for one, two, three, four, five and six days, respectively. Six similar, nonirradiated rats served as controls. All histologic procedures were carried out in duplicate, and microscopic examination was made of the cardiac and pyloric portions of the stomach, the small intestine at distances of 5, 10, 15 and 20 inches from the stomach, the cecum, and the colon at a distance of 2 inches from the cecum. Numerous staining methods were used, especially van Gieson, Nile blue for bacteria, and carbol thionin with iodine for mucus.

In the cecum the first pathologic changes noted after forty-eight hours' exposure consisted in a great increase of mucinogen granules in the cells lining the tubular glands; the granules occupied clear vacuoles in the cell protoplasm. This was not confined to the goblet cells, as in the normal formation of mucus, but was found in the columnar cells, was extensive and disorderly, and represented the first stage of mucoid degeneration. After three days' exposure the granules were less numerous but larger and the hyaline material was more abundant. The mucoid degeneration also involved the cells at the base of the glands. Few normal goblet cells were visible. After four days' exposure very few mucinogen granules were seen, and normal goblet cells were absent. The lumen of the glands was free from mucus, except at the base or at the mouth. The columnar cells stained more faintly than the cells of normal animals, and their nuclei were larger and less deeply stained. Little further change was found after five or six days' exposure. Small areas of desquamation of the columnar cells, exposing the connective tissue, were noted occasionally.

MOTTRAM and KINGSBURY (1925) tried to ascertain experimentally whether exposure to radium or roentgen rays sufficient to cause thrombopenia was associated with the presence of intestinal bacteria in the blood stream, or whether lowering the animal resistance to bacterial infection by irradiation could account for the septicemia. Seven rats were exposed to sufficient radiation[118] to produce thrombopenia, and five nonirradiated rats were used as controls. Cultures from the heart-blood were made by incubating 0.5 c.c. of blood with 20 c.c. of broth at 37° C. Anaerobic cultures were also made, with negative result. All the aerobic cultures from the control animals were negative, while those from the irradiated animals were positive, and showed coliform bacilli, diphtheroid bacilli, sarcinae and staphylococci.

To test the general resistance of irradiated animals, a series of rats was inoculated subcutaneously with anthrax, but no difference between the irradiated and control animals was found. Six irradiated and six nonirradiated rats were inoculated in the peritoneum with *Bacillus tuberculosis* (old bovine strain).[119] A month afterward the bacillus was found in the mesenteric glands of the irradiated animals, and microscopic tubercles were found in three

[117] Ra $Br_2 2H_2O$; distance, 8 in.; filtration: 0.1 mm. of lead and 0.12 mm. of silver. It is not clear how irradiation was carried out.

[118] The rats were exposed to radium; the guinea pigs to roentgen rays generated at a voltage equivalent to a spark-gap of 18 cm. No other technical details were given.

[119] 0.5 c.c. of a suspension containing 150 by 10^6 bacteria per cubic centimeter.

of them; a similar condition was found in one of the control animals. *Bacillus coli* from the heart-blood of an animal used in the first series of experiments was inoculated into the saphenous vein of six irradiated and of six nonirradiated rats. The results were the same in both groups. In another series, *Bacillus coli* was inoculated into four irradiated and two nonirradiated rats, but there was no difference in the results. All the animals in the last series remained alive and healthy, although anemia was perceptible six days after inoculation.

Two rats were inoculated until the platelets fell to 123,000 and 33,000 per cubic millimeter, respectively. Five million *Bacillus coli* were then inoculated into the saphenous vein. Twenty hours later the heart-blood of one animal contained many *Bacillus coli*, but there were no polymorphonuclear cells and very few platelets; the heart-blood of the other rat contained some bacteria, a few polymorphonuclear cells, but no platelets. After twenty-four hours, smears from a discharge from the eyes showed *Bacillus coli* and a diphtheroid bacillus. These rats died forty-three and forty hours, respectively, after inoculation. The spleen and lymph nodes showed great destruction of erythrocytes; there were bacteria in the spleen and in the vessels around a lymph node, but none within the node. In one nonirradiated, control rat, with platelets numbering 1,130,000, there were no bacteria and few platelets and polymorphonuclear cells in smears from the heart-blood made two hours and twenty hours after inoculation. In another control animal, with a platelet count of 1,160,000 per cubic millimeter, there were a few bacteria and platelets in smears from the heart-blood an hour after inoculation; there were no bacteria or platelets and only a few polymorphonuclear cells two hours after inoculation. In the eyes of the first control rat a discharge developed forty-eight hours after inoculation. At the end of seven days, the rat became very ill and anemic, and was killed. The spleen, liver and bone marrow showed massive round-cell regeneration, and the blood contained many nucleated erythrocytes. The second control rat died twenty-four hours after inoculation from pericardial and mediastinal hemorrhage (heart puncture).

Four guinea pigs, weighing between 420 and 460 gm., were irradiated sufficiently to produce mild thrombopenia; four other pigs were not irradiated and served as controls. All were inoculated with *Staphylococcus aureus* from a case of osteomyelitis. One irradiated animal died forty-eight hours later with abscesses in the liver, spleen and kidneys; the three others remained well and, with the control animals, were again irradiated and inoculated intraperitoneally with *Bacillus paratyphosus*. The irradiated, and one of the control, animals died three, eight, four and thirty days, respectively, after inoculation. *Bacillus paratyphosus* was recovered at necropsy in all cases. Mottram and Kingsbury thought it possible that the greater susceptibility of the irradiated animals in the last experiment may have been due to excessive thrombopenia caused by the second irradiation.

To test the effect of irradiation on the production of immune substances, three rats were irradiated until mild thrombopenia was produced, and the fragility of the erythrocytes was compared with that of three nonirradiated, control animals.[120] The fragility of the erythrocytes was not decidedly altered by exposure to radium. Tests for complement fixation and for opsonins[121] did not show any essential difference between the irradiated and the nonirradiated rats and guinea pigs.

From these experiments, which showed that irradiation to the point of mild thrombopenia was associated with the presence of intestinal bacteria in the blood stream and that such exposure has little or no influence on the resistance of the animal to bacterial invasion or on antibody production, Mottram and Kingsbury concluded that the presence of intestinal bacteria in the blood stream of irradiated animals is due to leakage of bacteria through the intestinal mucosa and probably accounts for the thrombopenia which follows irradiation.

[120] Blood withdrawn from the heart into citrate solution, and thrice washed with a solution of normal sodium chloride; 0.025 c.c. of packed corpuscles was placed in tubes containing 2.5 c.c. of sodium chloride solution. Readings were made after one hour at room temperature.

[121] Wright's technique.

Analysis of Experimental Data

Roentgen Rays. The foregoing experiments show that small doses of roentgen rays have no effect on the small intestine, but that largè doses may cause slight or severe clinical manifestations of intestinal irritation or injury and more or less marked and extensive pathologic changes. In other words, the intestine is able to tolerate irradiation within certain limits, but when the limit of physiologic tolerance is exceeded, evidences of irritation or injury become apparent. The symptoms caused by excessive irradiation may be slight and consist in transient anorexia, with or without loss of weight; or they may be severe and characterized by anorexia, vomiting, loss of weight, general depression and diarrhea often ending in death, and these disturbances may be associated with more or less marked pathologic alterations. The severity of the clinical disturbances and the degree of the pathologic changes, which appear to be most marked in the duodenum and jejunum, are proportional to the intensity of irradiation, and their extent to the dimensions of the territory exposed. In analyzing the experiments it is necessary, therefore, to take into account the technical conditions of irradiation which govern the dose and the area of body exposed. The effect of variation in dosage is well illustrated by the experiments of Krause and Ziegler (1906–1907), and Keller (1921), which show that, while the leucocytes of the blood and the lymphocytes in the spleen, lymph nodes and intestinal lymph follicles undergo extensive degeneration after small as well as large doses. clinical disturbances and pathologic changes characteristic of intestinal irritation or injury occur only after strong doses.

It is to be expected that the clinical and pathologic disturbances should vary at least as much as the experimental conditions; and since great variation in these conditions is apparent in the different experiments, it is not surprising that the effects noted should vary just as greatly. The doses of roentgen rays used in most of the experiments were much larger than the doses used in treating human beings, without allowance for the difference in the size of the animals and man. If such allowance is made, the doses are even more disproportionate. That many of the animals were able to survive such strong irradiation proves that the intestine possesses a good measure of resistance; but that others succumbed shows that irradiation beyond the limit of such resistance may be fatal. The extent of intestinal injury is probably as important, if not more important, in the ability of the organism to survive, as the degree of injury at any single point.

Evidence indicates that the sensitiveness of the small intestine is greater than that of the stomach, which remained organically unaffected in all the experiments except those of Regaud, Nogier and Lacassagne, in which direct exposure of the stomach caused changes in this organ; it is also indicated that the small intestine is more sensitive than the large intestine, which showed only slight changes or none at all. In the experiments of Denis, Martin and Aldrich, it is true, there was evidence of organic injury in the large intestine, and none in the small intestine, but this was probably due to the manner of irradiation in which more of the large than of the small intestine was exposed. In corroboration of this the clinical symptoms of intoxication appeared later in their experiments and were not so marked as in the experiments of Warren and Whipple (1922), and Martin and Rogers (1923–1924), in which the symptoms of intestinal irritation were severe, appeared early, and the correspondingly marked pathologic changes involved chiefly the small intestine.

The pathologic changes in the intestine resulting from irradiation consist in: increase in tonus and spastic contraction of the bowel; mucoid and vacuolar degeneration, desquamation and disappearance of the intestinal epithelium; hyperemia, leucocytic infiltration, hemorrhagic and fibrinous exudation of the mucosa; atrophy or sloughing of the denuded villi; edema of the submucosa; atrophy of the glands of Lieberkühn, and sometimes ulceration of the mucosa; regeneration of the epithelium and proliferation of the connective tissue. The doses of roentgen rays were often so strong and the resulting changes so marked that it is difficult to determine the relative order of these changes. However, the experiments of Swan (1924) on isolated pieces of intestine suggest that increase in the tonus of the bowel is the initial step in the reaction to irradiation. The observation of spastic contraction of the intestine by Hall and Whipple (1919) is probably to be regarded as an exaggerated increase in tonus resulting from actual injury, and is undoubtedly analogous to the spastic phenomena incident to other forms of intestinal irritation or injury. The increase in tonus was observed by Swan after small doses of roentgen rays to isolated pieces of intestine; the tonus returned to normal after irradiation ceased. This effect and the slightly greater spastic contraction noted by Hall and Whipple probably represent the earliest phase in the reaction of the bowel to irradiation. Mucoid degeneration of the intestinal epithelium is an early and constant observation, and the experiments of Mottram with radium indicate that it represents the first phase in the cellular degeneration caused by irradiation. It seems likely that this mucoid degeneration of the epithelium and accumulation of mucus in the intestine, so frequently noted, interferes with the absorption of water and food materials and may explain, in part at least, the loss of weight so common in animals after exposure of the abdomen to roentgen rays. After stronger doses the epithelial cells lining the intestine desquamate and are thrown off into the intestinal canal, an observation amply substantiated by the experiments of Krause and Ziegler (1906–1907), Regaud, Nogier and Lacassagne (1912), Fromme (1917), Hall and Whipple (1919), Denis, Martin and Aldrich (1920), Keller (1921), Warren and Whipple (1922), Martin and Rogers (1923), Podestà (1925), Tzusuki (1926), and Domagk (1927). This effect is not uniform throughout the intestine, certain portions of which are injured much more than others. The experiments of Hall and Whipple (1919) and Warren and Whipple (1922) indicate that the epithelium lining the intestinal crypts is more sensitive than that covering the villi. This observation was not confirmed by Martin and Rogers (1924), who found the epithelium of the crypts well preserved when the mucosa had not sloughed completely. The reason for such discrepancy is not clear, unless it is related to the failure of these authors to make any observations during the first four days following irradiation. These changes are always associated with hyperemia, more or less leucocytic infiltration, and hemorrhagic or fibrinous exudation of the denuded surface of the villi and sometimes also of the underlying stroma. Some of the villi undergo atrophy or slough away, and the submucosa becomes edematous. Actual ulceration of the mucosa has been described by Regaud, Nogier and Lacassagne (1912), Martin and Rogers (1924), and Podestà (1925). Hall and Whipple (1919), and Warren and Whipple (1922) have also shown that the rate of autolysis of the intestine is greatly increased after irradiation sufficient to cause degenerative changes in the mucosa of the bowel, such as described by them.

Later, regeneration occurs and its character and progress depend on the degree

of the initial injury. Regeneration of the epithelium may be complete if the antecedent degeneration was only slight or moderate; or the epithelium may not regenerate and the reparative process may be characterized partly or largely by connective tissue replacement if the initial injury was severe. Such connective tissue proliferation may be quite marked and lead to shortening and constriction of the irradiated segment of bowel, as shown by the experiments of Martin and Rogers (1923) on isolated loops of small intestine. Indeed it may give rise later to obstructive phenomena, but such constrictions and shortening from essential scar formation must not be confounded with the increase in tonus noted by Swan (1924) and the spastic contraction mentioned by Hall and Whipple (1919). The former are probably the earliest effects of irradiation on the bowel, while the latter are the final stage of repair of severe injury. For a time after strong doses, on the contrary, reparative proliferation of fibroblasts may be retarded, as shown by the observations of Martin and Rogers (1924), whose experiments led them to conclude that the mucosa of the small intestine is approximately twice as sensitive to irradiation as the mucosa of the stomach.

Krause and Ziegler (1906–1907), Keller (1921) and Warren and Whipple (1923) have described a marked accumulation of bacteria on the surface of the intestinal mucosa denuded of its epithelial covering by strong irradiations. Keller, and Warren and Whipple studied this phase of the reaction by bacteriologic methods. Keller found an abundance of colon bacilli in the heart-blood and feces. Thinking that this meant an abnormal invasion of the blood stream by bacteria, which had been enabled to pass from the intestine into the blood on account of the destruction of the intestinal epithelium by irradiation, Keller fed *Bacillus prodigiosus* to some of his animals, by enema and through a stomach tube, but was unable to recover the organism from the blood or feces. Warren and Whipple also attacked this problem bacteriologically, but evidence of bacterial invasion was never obtained from the heart-blood until shortly before death. Their natural conclusion was that an overwhelming bacterial invasion of the tissues, lymph or blood does not follow extensive destruction of intestinal epithelium by strong irradiation of the abdomen, and that the intestinal epithelium is not an indispensable barrier against intestinal bacteria, as has generally been supposed. This interesting point will be considered further in connection with the experiments of Mottram (1923) and Mottram and Kingsbury (1925) which, although carried out partly with roentgen rays and partly with radium, will be dealt with under radium.

Exposure of the human body to roentgen rays commonly causes systemic reaction, the symptoms of which are anorexia, nausea and vomiting. The degree and duration of this reaction, which appears a few hours after exposure and lasts from a few hours to several days, varies with the area of body surface exposed and the dose of irradiation. A few patients escape it altogether, usually because the total dose administered has been small, but some persons have a much greater tolerance to irradiation than others. This systemic reaction is of such constant occurrence in the practice of radiotherapy that much thought has been given to its etiology and prevention. Many hypotheses have been advanced to account for the phenomenon, but thus far none of the explanations put forth or none of the experiments undertaken to substantiate these explanations has been sufficiently convincing to command acceptance.

Several of the foregoing investigators have seen in the results of their experiments what they considered a satisfactory solution of the problem of radiation sickness. Thus Hall and Whipple (1919) regarded the systemic reaction in dogs and the pathologic changes in the intestine after irradiation of the abdomen as akin to the intoxication caused by intestinal obstruction. This is a sound deduction, but their conclusion that the pathologic alterations in the small intestine are the probable cause of the nonspecific reaction which often follows irradiation is of doubtful validity, because the same systemic reaction, in human beings at least, occurs after exposure of regions remote from the abdomen. It is true that the reaction resulting from abdominal irradiation is usually more severe than that which follows irradiation of other regions, but the difference is only of degree. Denis, Martin and Aldrich (1920) pointed out that some of the rabbits whose reaction was particularly severe did not show any intestinal lesions, and they suggested that the intestinal abnormalities noted in other animals by Hall and Whipple and by them may have been the result rather than the cause of the systemic intoxication. The evidence furnished by all these different experiments contradicts such an assumption. There can hardly be any doubt that strong irradiation of the intestine is the direct cause of the organic abnormalities described, and also of the clinical symptoms of intestinal irritation.

The experiments of Hall and Whipple, and Warren and Whipple, show that the doses of radiation were exceptionally strong by reason of converging beams. Nevertheless, no untoward symptoms developed until from twenty-four to forty-eight hours had elapsed. The symptoms increased in severity and reached a climax on the fourth day after irradiation, when the animals died or were killed to anticipate impending death. This sequence of events is quite different from that which characterizes true radiation sickness. In the latter the reaction appears within a few hours, is worst at or soon after the onset and then subsides gradually. This difference appears fundamental and probably indicates that, while the symptoms of severe intestinal injury caused by direct irradiation of the bowel and those of true radiation sickness are of the same general nature, their cause is partly or entirely different.

Therefore, the explanation offered by Hall and Whipple, that the clinical disturbances and pathologic changes in the intestine which follow irradiation of the abdomen beyond the tolerance of the bowel resemble the intoxication caused by intestinal obstruction, deserves serious consideration. It is not a question of obstruction but of injury from any cause. Additional evidence of this is found in the circumstance that the duodenum and jejunum are more susceptible to the action of the rays than the remainder of the intestinal tract. It is well known that the intoxication resulting from injury of the upper portion of the small intestine is always more severe than when such injury involves the lower part of the bowel. However, while we may accept this partial explanation provisionally, it cannot be interpreted as a solution of the etiology of radiation sickness. The direct effect of irradiation on the intestine may complicate and add a note of confusion to the manifestations of radiation sickness, but cannot serve as a general explanation of such reaction, which occurs after irradiation of regions remote from the abdomen. One must conclude, therefore, that the clinical disturbances and organic alterations resulting from direct exposure of the intestine are essentially separate and distinct from the systemic reaction occurring after irradiation of other parts of the body. The gastrointestinal tract of animals and of man reacts differently to certain factors. Few animals, for exam-

ple, become sea-sick. This may be due to differences in the character of food, but probably also to essential differences in the anatomy and physiology of the digestive tract, and may account for the failure of Warren and Whipple, and Martin and Rogers to observe any clinical disturbance after irradiating the thorax of dogs, or to find any abnormality in the intrathoracic structures at necropsy. Dogs certainly differ in this respect from human beings, who almost always experience slight or pronounced radiation sickness after exposure of the thorax, neck and other regions in which the intestine cannot possibly be implicated.

The doses of roentgen or radium rays used in treating human beings are seldom sufficient to irritate the intestine in the manner described, but, as will be seen later, intestinal irritation and injury sometimes occur after exceptionally strong irradiation, and many accidents of this kind have been reported; every therapeutic radiologist encounters such complications in attacking certain resistant abdominal tumors with strong doses of roentgen rays. Ceresoli's observation of hyperglycemia after irradiation of portions of the abdomen (intestine) remote from the pancreas and liver is interesting, but his failure to describe the precise technical conditions under which this observation was made precludes analysis.

Radium. The experiments of Löhe and of Mayebo show that thorium X injected intravenously causes hyperemia of, and petechial hemorrhages in, the mucosa of the intestine and in the kidneys. The pathologic changes in the intestine are most marked in the large bowel, and they vary in severity and extent according to the dose injected. After large doses petechial hemorrhages may be numerous and may coalesce, and coagulated blood may be found in the colon. The small intestine may show similar changes, but they are less pronounced than in the large bowel, in which the crests of the intestinal folds may appear intensely hemorrhagic. Nearly all the animals died; the others would probably have died also had they not been killed so soon after injection. These experiments indicate that thorium X injected intravenously is excreted largely, if not entirely, through the kidneys and bowel. The experiments of Mayebo are of special interest, because they apparently explain why the large intestine is affected much more than the small intestine and kidneys; his conclusion that the greater severity of the lesions in the colon is due to the longer time allowed for the action of thorium by the slow movement of the contents of the large bowel appears entirely justified.

It is worthy of note that in these experiments mucoid degeneration and accumulation of mucus in the bowel also was one of the earliest effects of irradiation. Indeed, in some of the animals injected with thorium X, accumulation of mucus in the intestine was the only change noted. That this represents an early stage in the reaction is shown by the circumstance that such animals had received relatively small doses, and that those which had received larger doses presented, not only accumulation of mucus, but also hyperemia and petechial hemorrhages.

The action of radium on the intestine is the same as that of roentgen rays. Ample evidence of such similarity of action is to be found in the experiments of Lazarus-Barlow and to some extent also in those of Mottram, although the studies of the latter related chiefly to a subsidiary phase of the problem. Mucoid degeneration was a prominent feature of the pathologic changes described by Lazarus-Barlow and the outstanding feature of Mottram's experiments. Altogether, the evidence strongly supports the conclusion that mucoid degeneration of the intestinal epithelium con-

stitutes an early phase of the reaction of the intestine to roentgen and radium irradiation. The marked increase in mucinogen granules in the goblet and columnar cells lining the tubular glands, the swelling of many of the cells with mucus, and the abundant outpouring of mucus into the lumen of the intestine, described by Mottram and noted by most of the investigators, indicates that epithelial cells which secrete mucus are exceptionally sensitive. According to Mottram, mucoid degeneration occurs during the first few days which follow irradiation. For a time after this little mucus is secreted; this undoubtedly represents the inhibitory phase of reaction. Later still, as the epithelial cells regenerate the production of mucus may return to normal or, if the dose of rays was sufficiently large, the secretion of mucus may remain deficient for a long time.

Mottram's deduction that the thrombopenia and anemia which sometimes follow irradiation may be due to mucoid degeneration of the intestinal epithelium and toxemia from absorption of intestinal bacteria need not concern us here; this point will be dealt with elsewhere. But the possible invasion of the blood stream by intestinal bacteria as the result of extensive destruction of the intestinal epithelium by radiation is most important. Mottram reported having found bacteria adhering to the injured mucosa and invading the underlying connective tissue in some of his irradiated animals; this observation led him to ascribe part of the toxemia occurring after irradiation to absorption of intestinal bacteria. He inferred that such bacterial invasion occurs only "after irradiation sufficient to produce thrombopenia," which, on the basis of his experiments, should mean irradiation sufficient to produce mucoid degeneration of the intestinal epithelium.

In connection with the action of roentgen rays on the intestine, Krause and Ziegler, Keller, and Warren and Whipple also had noted masses of bacteria covering the injured and denuded surface of the bowel. Keller found colon bacilli in the heart-blood of some of his animals. Warren and Whipple never found evidence of bacterial invasion of the blood stream until shortly before death, and regarded this as analogous to the invasion occurring as a terminal event in unirradiated animals. Mottram and Kingsbury, on the contrary, obtained positive blood cultures from all irradiated animals and none from the unirradiated control animals. The apparently sharp contrast between the results obtained by Warren and Whipple, and Mottram and Kingsbury might possibly be explained if we knew the relation of the cultures made by the latter to the death of their animals. Unfortunately, such information is not available, and the point must remain unsettled. Notwithstanding this apparent conflict in results, so far as the blood cultures are concerned, Mottram and Kingsbury agree with Warren and Whipple in showing that body resistance to infection is not affected appreciably by irradiation. Their experiments indicate that injury to the intestinal epithelium by roentgen or radium rays does not increase the susceptibility of animals to infection and, therefore, that the intestinal epithelium is not an indispensable barrier to invasion of the blood stream by the bacterial residents of the intestine.

Clinical Considerations

Roentgen Rays. The only clinical bearing of roentgen irradiation on the intestine is the possibility of inducing symptoms of enteric irritation or of actually injuring the bowel. Previous to 1918 several authors, such as Regaud, Nogier and Lacassagne (1912), and Albers-Schönberg (1913), had called attention to the danger of in-

testinal injury from excessive irradiation. These warnings were based on the results of animal experiments, but, although the circumstances leading to these experiments are not mentioned,it is quite possible that the idea of undertaking them may have originated in clinical observation of gastrointestinal disturbances that suggested irradiation as the causal factor. In any event, no record of intestinal irritation or injury by roentgen rays is to be found until 1917, when FRANZ and ORTH cited the case of a woman aged thirty-five years, in which diarrhea developed after each of three courses of irradiation for carcinoma of the uterine cervix. At necropsy, swelling and extensive necrosis of the intestinal mucosa, and multiple ulcers were found, and there were masses of bacteria in the areas of necrosis and in the submucosa. In commenting on this case, FLATAU explained that the intestinal injury with the formation of fistula was due to inflammatory reaction of the peritoneum to the severe necrosis of the abdominal wall, which was the result of excessive irradiation. Nevertheless, Flatau's statement that the intestinal disturbance in this case was "not caused primarily by hard x-ray irradiation" represents extraordinary reasoning. Flatau undoubtedly meant that the case could not be classified with those in which functional or organic disturbance of the intestine occurs without any sign of irritation in the skin and subcutaneous tissues.

VON FRANQUÉ (1918) reported the case of a woman who had been exposed to irradiation on three separate occasions for hyperplastic endometritis. The two first courses of irradiation had not had any undesirable effect, although the dose had been fairly strong. Almost three months later a third course was given through the lower part of the abdomen and back, and the dose was increased about 20 per cent. Extensive radiodermatitis of the right side of the abdomen appeared two weeks afterward; vomiting, meteorismus, and profuse, watery diarrhea accompanied by severe colic soon followed. The symptoms subsided slowly, but the abdomen was still distended a month later. According to the author, "There was no question that she was suffering from severe enteritis due to the irradiation." She improved slowly, but had not fully recovered when the report was prepared. HECK (1920) gave the subsequent history of the case reported in 1918 by von Franqué, in which intestinal fistula with infection of the abdominal wall developed. An attempt was made to deal with this surgically, but gangrene of the wound, peritonitis and intestinal ileus resulted, and the patient died.

It may be recalled that the therapeutic use of highly penetrating roentgen rays of short wave-length generated at high voltage became general during this period, and since then clinical evidence of intestinal injury from irradiation has become more common. This is not surprising if we bear in mind the large doses advocated by many radiologists for the treatment of carcinoma of the uterus, rectum or other tumors within the abdomen. HAENDLEY (1921) published a long list of cases in which various parts of the bowel had undergone more or less severe injury from roentgen irradiation. His communication included the necropsy observations and the microscopic appearance of the injured intestine in each case. Haendley pointed out pertinently that while the dose given to each separate field treated may not have been excessive, the intestinal lesions described constitute sufficient proof that the convergence of several beams of roentgen rays on one portion of the abdomen or pelvis must have made a total dose excessive enough at some internal point to have caused the injury.

Fischer (1922) cited three interesting cases of intestinal injury. The first shows clearly that irradiation of the abdomen to the point of second degree radiodermatitis not only caused the bowel to adhere to the injured area of the abdominal wall but extensive destruction of intestinal epithelium and ulceration of the mucosa. This resembled in every respect the injury of the bowel produced experimentally in animals. The two other cases show that converging irradiation of the abdomen through several fields, even though the dose to each field may not be sufficient to cause radiodermatitis, may cause severe intestinal injury and death. The only possible explanation is that the dose at the point of convergence of the several beams of rays within the abdomen must have exceeded the physiologic limit of tolerance of the involved portion of the intestine.

Besides those mentioned, many other cases of intestinal injury from excessive exposure of the abdomen to roentgen rays have been recorded by Fried (1922), Mathias (1922–1923), Mühlmann and Meyer (1923), Schwarz (1923), Glaser (1924), Sanders (1924), and others. The authenticity of some of the cases reported is not absolute, but in a larger number the relationship between irradiation and intestinal injury cannot be questioned. It is worthy of note that the majority of such reports have emanated from German sources; this must undoubtedly be related to the use, by many German radiologists, of strong, or so-called massive, doses of roentgen rays in dealing with resistant tumors, such as carcinoma of pelvic or abdominal structures.

The only possible conclusion to be drawn from the foregoing reports is that irradiation of the abdomen to the point of marked radiodermatitis through a single field, or to a point at which the skin remains unaffected when several beams of radiation converge toward a common internal point, may give rise to manifestations of intestinal irritation or injury. Such disturbances may disappear without leaving any functional or organic trace if the tolerance of the intestine has been exceeded only slightly, or it may be followed by pronounced pathologic changes entailing more or less serious disability, or even death if such tolerance is grossly exceeded. Ordinary therapeutic doses do not produce such effects.

Radium. Instances of intestinal irritation or injury by radium or products of radium actually preceded such incidents after roentgen irradiation. Thus Gudzent (1912) noted diarrhea, abdominal pain and vomiting in a patient with arthritis treated by intravenous injections of thorium X. As may be seen from the experiments on animals the intravenous administration of thorium X affects chiefly the large bowel and kidneys, which are the main excretory pathways of this substance. Schauta (1914) reported the constant incidence of loss of weight, cachexia, diarrhea, tenesmus, fever, vomiting, headache, loss of appetite, decrease of hemoglobin and erythrocytes in the first of three groups of patients who had received excessive doses of radium. Necrosis, fistulas, mucopurulent and purulent inflammation of the bladder and of the large and small intestine were found at necropsy. No such clinical manifestations or pathologic changes were noted in a third group of patients who had been irradiated with smaller doses. Schweitzer (1914), Krecke (1915), Füth and Ebeler (1915), Weishaupt (1918), Eckelt (1919), Benthin (1921), Coulomb and Jean (1922), and others have cited similar effects from excessive exposure to radium or mesothorium. Most of these reports have been incidental to the use of radium or mesothorium in the treatment of carcinoma of the uterus, vagina or rectum.

Conclusions

Roentgen Rays. Experiments on animals show that the sensitiveness of the intestine to direct irradiation is greater than that of the stomach, and that doses of roentgen or radium rays beyond the limit of physiologic tolerance may cause slight or pronounced functional or organic disturbances in the bowel. The small intestine is more sensitive than the colon, and the duodenum and jejunum are the most susceptible portions of the small bowel. The clinical manifestations of excessive exposure of the intestine consist in anorexia, vomiting, loss of weight, diarrhea, and tenesmus, and death may ensue in extreme cases. The severity of the symptoms varies, naturally, with the degree of over-exposure.

The pathologic changes in the intestine caused by irradiation beyond the tolerance of the bowel are characterized by: increase in tonus or spastic contraction of the intestine; mucoid degeneration, vacuolization, and desquamation of the intestinal epithelium, beginning first in the cells overlying the lymph follicles and those lining the crypts, and extending later to the epithelial investment of the villi; atrophy or disappearance of the villi; hyperemia, edema and sometimes ulceration of the mucosa; accumulation of bacteria on the denuded surface of the mucosa or in the stroma itself; leucocytic infiltration; regeneration of the mucosa in the injured portions of the bowel or proliferation of connective tissue to replace collections of cells injured beyond possible regeneration.

The mucoid degeneration of the intestinal epithelium is probably responsible, in part at least, for the loss of weight through interference with the absorption of water and food.

The clinical disturbances caused by excessive irradiation of the bowel constitute a specific reaction, which, although of the same general character as the common nonspecific reaction known as radiation sickness, differs essentially from it and is a separate and distinct process.

Exposure of the intestine to excessive doses of roentgen rays in connection with the treatment of various pathologic lesions in human beings may cause clinical disturbances or changes characteristic of enteric irritation or injury. Many instances of such effects have been reported.

Radium. Thorium X injected intravenously is excreted largely through the intestinal and urinary tracts, and gives rise to mucoid degeneration of the intestinal epithelium, and to hyperemia and hemorrhage in the large intestine and kidneys.

The action of radium on the intestine is the same as that of roentgen rays. Many cases have been recorded in which excessive exposure to radium has led to clinical symptoms of intestinal irritation or to actual ulceration of the bowel. As might be expected, such complications have arisen chiefly from the use of radium in treating carcinoma of the uterus, bladder or rectum.

The accumulation of bacteria on the denuded mucosal surface of the bowel and bacterial invasion of the underlying stroma has been related, on the one hand, to the thrombopenia which sometimes follows irradiation and, on the other hand, to the presence of bacteria in the blood stream of irradiated animals after death. The relation to thrombopenia of the bacteria on or in the injured mucosa of the bowel after irradiation has not been definitely established, and Warren and Whipple have apparently shown that bacterial invasion of the blood stream occurs only as a terminal or agonal phase.

To be continued.